Archives of Neurology and Psychiatry

VOLUME 34 SEPTEMBER 1935 NUMBER 3

FUNCTIONAL CHANGES IN THE BRAIN OF THE DOG AFTER REDUCTION OF CEREBRAL BLOOD SUPPLY

I. CEREBRAL CIRCULATION AND THE DEVELOPMENT OF ANASTOMOSIS AFTER LIGATION OF THE ARTERIES

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The effect of changes in the circulation of the blood on the activity of the brain has been the subject of many experiments, from the classic examples (Cooper,[1] in 1836, and Kussmaul and Tenner,[2] in 1857) up to more recent work, such as that of Pike, Guthrie and Stewart[3] (1906), Crile and Dolley[4] (1908), Gildea and Cobb[5] (1930) and Petroff[6] (1931). The changes in the somatic functions of the brain and medulla oblongata during acute anemia were particularly observed. Anemia was produced by means of temporary or permanent ligation of the arteries supplying the brain, by temporary arrest of the heart action or by injection of substances causing thrombosis of the arteries (Couty[7] [1887]—lycopodium; and Markwald[8] [1890]—wax). Usually the animals that survived acute anemia were observed only for short periods at intervals of a few hours or days. Changes in the higher

From the Department of Physiology, McGill University, Montreal, Canada.

1. Cooper, A.: Some Experiments and Observations on Tying the Carotid and Vertebral Arteries, Guy's Hosp. Rep., no. 1, 1836.

2. Kussmaul, A., and Tenner, A.: Untersuch. z. Naturlehre **3**:1, 1857; quoted by Petroff.[6]

3. Pike, F. H.; Guthrie, C. C., and Stewart, G. N.: Studies in Resuscitation, J. Exper. Med. **8**:289, 1906; **10**:490, 1908; Studies in Resuscitation, Am. J. Physiol. **17**:344, 1906; **19**:328, 1907; **20**:61 and 407, 1907; **21**:359, 1908; **22**:51, 1908.

4. Crile, G., and Dolley, D. H.: On the Effect of Complete Anaemia of the Central Nervous System in Dogs Resuscitated After Relative Death, J. Exper. Med. **10**:782, 1908.

5. Gildea, E. F., and Cobb, S.: The Effects of the Anemia on the Cerebral Cortex of the Cat, Arch. Neurol. & Psychiat. **23**:876 (May) 1930.

6. Petroff, J. R.: Experimentelle Untersuchungen über die Funktionsstörungen der Nervenzentren bei Gehirnanämie, Ztschr. f. d. ges. exper. Med. **75**:1, 1931.

7. Couty, quoted from Pekor, W.: Ueber pathologisch-anatomische Veränderungen der Hirnelemente bei künstlich hervorgerufener Blutarmut, Dissert., St. Petersburg, 1887.

8. Markwald: Ztschr. f. Biol. **26**:259, 1890; quoted from Hill, L.: The Physiology and Pathology of the Cerebral Circulation, London, J. & A. Churchill, 1896.

nervous activity which developed as a result of disturbances in the cerebral circulation were studied simply by observing the general behavior of the animal. Consequently the finer functional changes in the brain were liable to escape the attention of the experimenter.

Cooper (1836), L. Hill [9] (1900) and others showed that after ligation of the two carotid and the two vertebral arteries disturbance in the mental processes developed in some animals. During the first week after the operation Hill's dog behaved in the same way as Goltz' dog from which the hemispheres had been removed; i. e., it acted like "a complete idiot." Two weeks after the operation, however, these disturbances disappeared, and the dog became practically normal. Pike, Guthrie and Stewart (1908) reported that "after long occlusion, apparent insanity had been seen, and in one case a total loss of the mental processes occurred." Gildea and Cobb (1930) observed similar disturbances in the intelligence of cats after tying of the arteries for a period while the animals were recovering from an operation. Histologic examinations of the brains of the animals thus operated on have shown that changes take place in the cells of the gray matter following acute anemia. These changes, depending on the duration and degree of the anemia, were of different grades. Chromatolysis, swelling, fragmentation, homogeneous staining and finally complete necrosis of the nerve cell were observed (the "areas of devastation" of Gildea and Cobb). The large and small pyramidal cells are the most susceptible to anemia. The cells in the medulla are more resistant (Hill and Mott [10] [1906], Gomez and Pike [11] [1909] and others). Thus, the loss of intelligence in acute anemia could be explained by the histologic changes in the gray matter of the brain.

If the cortical cells are more susceptible to cerebral anemia, it would appear to be possible to change the cerebral circulation and produce degeneration of the cortex without injuring the subcortex and medulla oblongata. The method of anemia seems to be better than that of surgical intervention, which is a relatively rough, mechanical procedure to apply to an organ of exquisitely delicate structure and function.

My aim was to produce degeneration of the cortex by restriction of the cerebral circulation and to study the character of the functional

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9. Hill, L.: On Cerebral Anaemia and the Effects Which Follow Ligation of the Cerebral Arteries, Tr. Roy. Soc. London, s.B **193**:69, 1900.

10. Hill, L., and Mott, F. W.: The Neurofibrils of the Large Ganglion Cells of the Motor Cortex of Animals in Which the Four Arteries Have Been Ligatured, Proc. Physiol. Soc., London **34**:iv, 1906.

11. Gomez, L., and Pike, F. H.: The Histological Changes in Nerve Cells Due to Total Temporary Anaemia of the Central Nervous System, J. Exper. Med. **11**: 257, 1909.

Data for Experiments on Twenty-Four Dogs

Dog	Age	Arteries Ligated	Time of Survival After Ligation	Cause of Death
1	1 month	Both common carotid and both vertebral tied	20 days	Distemper
2	1 month	Both common carotid and both vertebral tied	12 hours	Died with symptoms of bulbar anemia
3	1 month	Both common carotid and both vertebral tied	12 hours	Died with symptoms of bulbar anemia
4	1½ months	I. 3/16/32: Both common carotid and both vertebral tied II. 10/24/33: Common carotid (just below origin of superior thyroid artery), occipital, internal and external carotid tied on right side; the parts of the arteries between the ligatures were excised III. 11/14/33: Left vertebral and its terminal branches tied from behind IV. 11/28/33: Right vertebral and its terminal branches tied from behind V. 12/12/33: Common carotid (just above origin of superior thyroid artery), occipital, internal and external carotid and posterior auricular tied on left side; the parts of the arteries between the ligatures were excised The dog was examined by the method of conditioned reflexes during 22 months	22 months	Killed 1 month after fifth operation
5	2 months	Both common carotid, both vertebral and both internal carotid tied	4 hours	Died with symptoms of bulbar anemia
6	12 weeks	Both common carotid and right vertebral tied	2½ months	Distemper
7	2½ months	Innominate, subclavian, common carotid and vertebral tied on right side	21 hours	Died with symptoms of bulbar anemia
8	2½ months	I. 5/25/32: Subclavian, common carotid, vertebral, costocervical trunk and omocervical trunk on right side tied and excised II. 10/31/33: Common carotid and vertebral on left side tied and excised III. 11/21/33: Both vertebral tied and cut from behind IV. 12/19/33: Common carotid, occipital, internal and external carotid and auricular on both sides tied and cut The dog was examined by the method of conditioned reflexes during 19 months	19 months	Killed 21 days after fourth operation
9	4 months	Both common carotid and both vertebral tied and cut	2 weeks	Killed
10	4 months	Both common carotid and both vertebral tied and cut	6 hours	Died with symptoms of bulbar anemia
11	4 months	Both common carotid and both vertebral tied and cut	22 hours	Died with symptoms of bulbar anemia
12	3 years	I. 8/1/32: Innominate, subclavian, common carotid, costocervical trunk and vertebral tied on right side; left vertebral tied and cut II. 8/23/33: Left common carotid tied and excised	3 weeks	Anesthetic (died during second operation)
13	7 years	I. 8/5/32: Common carotid, innominate, subclavian, costocervical trunk and vertebral on right side tied and cut; left common carotid also tied and cut II. 10/12/32: Left vertebral tied and cut	13 months	Killed

Data for Experiments on Twenty-Four Dogs—Continued

Dog	Age	Arteries Ligated	Time of Survival After Ligation	Cause of Death
14	4 years	I. 8/9/32: Subclavian, common carotid and vertebral on right side tied and cut; left common carotid also tied and cut II. 9/20/32: Left vertebral tied and cut III. 10/10/32: External and internal carotid on right side tied and cut IV. 10/19/32: External and internal carotid on left side tied and cut	13 months	Killed
15	4 months	I. 9/26/32: Both common carotid and left vertebral tied and cut II. 10/25/32: Left subclavian and right vertebral tied III. 4/20/33: Left vertebral tied from behind	12 months	Killed
16	5 months	Both common carotid and both vertebral tied and cut	23 days	Distemper
17	9 years (approx.)	Both common carotid and both vertebral tied and cut	8 hours	Died with symptoms of bulbar anemia
18	4 years	Both common carotid and both vertebral tied and cut	5 hours	Killed
19	3 months	I. 1/25/33: Left vertebral tied from behind II. 4/13/33: Right vertebral tied from behind III. 5/28/33: Both vertebral and right common carotid tied and cut	7 months	Killed
20	5 years	Both common carotid, both vertebral, both internal carotid and both occipital tied and cut	4 hours	Killed
21	4 years	Both common carotid and both vertebral tied and cut in front and from behind	4 hours	Killed
22	2 years	Both common carotid and both vertebral tied and cut at the base of the neck; both common carotid also tied and excised above origin of superior thyroid artery; both internal and both external carotid and both occipital tied and cut	4 hours	Killed
23	4 years	I. 10/17/33: Both common carotid and left vertebral tied and cut II. 11/7/33: Both common carotid tied and cut above origin of superior thyroid artery; both internal and both external carotid and both occipital tied and cut; the parts of the arteries between the ligatures were excised III. 11/24/33: Both vertebral tied and cut from behind IV. 12/8/33: Right vertebral tied and cut in the neck The dog was examined by the method of conditioned reflexes during 3 months	3 months	Killed 39 days after fourth operation
24	1 year	I. 11/3/33: Both common carotid and left vertebral tied and cut II. 11/17/33: Both vertebral tied and cut from behind III. 12/1/33: Right common carotid tied and cut above origin of superior thyroid artery; internal and external carotid and occipital on right side tied and cut; the parts of the arteries between the ligatures were excised The dog was examined by the method of conditioned reflexes during 9 months	1 month	Anesthetic (died during third operation)

disturbances consequent on this restriction. The first part of the work was of an anatomic character and was devoted to the study of the conditions of cerebral circulation and the development of anastomosis after ligation of the arteries supplying the brain. In the second part of the work the effect of changes in the cerebral circulation on the higher nervous activity was studied by the method of conditioned reflexes. All the experiments were carried out on dogs. Before describing the results obtained in this investigation a brief review will be given of the effect of ligation of the four main arteries supplying the brain.

Simultaneous ligation of the four main arteries to the brain in the dog has been carried out many times and by many experimenters, all of whom obtained different results. Cooper (1836) obtained full recovery after ligation of both carotid and both vertebral arteries, the latter having been tied at their origin from the subclavian artery. Further investigations were carried out by Porta [12] (1845), Schiff [13] (1854), Kussmaul and Tenner (1857), Baum (1889), Strelkoff [14] (1926) and others. Hill (1900) expressed the belief that dogs can survive ligation of the four arteries for at least a few hours after the operation. Ljubomudroff [15] (1930) carried out simultaneous ligation of the four arteries in eleven dogs; three of them died within from eight to fifteen hours after the operation.

The nutrition of the brain after ligation of the two carotid and the two vertebral arteries takes place by means of vicarious enlargement of the collateral vessels and development of new anastomoses. Cooper showed that the most important anastomoses formed after ligation of these four arteries in the dog develop through the union of the inferior thyroid artery and the ascending cervical arteries and also between branches of the vertebral arteries and the internal and external carotid arteries on the level of the first and second cervical vertebrae. Hill, after making an injection into dogs post mortem, found a free anastomosis between a branch of the superior intercostal artery and the anterior spinal arteries. Other intercostal arteries and the deep cervical arteries also anastomosed with the anterior spinal arteries at each verte-

12. Porta, L.: Delle alterazioni patologiche delle arterie per la legatura e la torsione, esperienze et osservazioni, Milan, G. Bernardoni di Gio, 1845.

13. Schiff, M.: Ein akzessorisches Arterienherz bei Kaninchen, Arch. f. physiol. **13**:239, 1854.

14. Strelkoff, S.: Die Unterbindung der Arteria anonyma in der experimentellen und klinischen Pathologie im Zusammenhange mit der Lehre über den Kollateralkreislauf, Dissert., Permsky; Permsky m. j., supp., nos. 1, 2 and 3, 1926.

15. Ljubomudroff, A. P.: Ueber die Entwicklung der kollateralen Bahnen nach Unterbindung der Aa. carotides und Aa. vertebrales am Halse des Hundes, Ztschr. f. Anat. u. Entwcklngsgesch. **91**:452, 1930.

bral segment. The work of Lubomudroff must be particularly mentioned. This investigator found that the main anastomoses developed in the neck after ligation of the individual arteries supplying the brain, as well as after simultaneous ligation of both carotid and both vertebral arteries. Unfortunately in his investigation little attention was paid to the nutrition of the brain.

METHODS

Our investigation was carried out on twenty-four dogs. The operations were done under ether anesthesia without morphine. The arteries were tied with two ligatures and cut between the ligatures. In some cases part of the common carotid arteries was excised in different lengths. From the table it may be seen that the arteries were tied in different combinations, either all at once or in several stages. The intervals between the operations were from ten days to eighteen months. The common carotid arteries were tied 1 cm. above their origin from the innominate artery. The vertebral arteries were ligated either (1) at their entrance into the vertebral canal or (2) at their exit from the vertebral canal on the back, on a level with the first and second cervical vertebrae. In the latter case the terminal branches were also tied. The occipital and auricular posterior arteries were ligated at their origin from the common carotid artery and the internal maxillary artery, respectively. The length of life of the dogs after the operation varied from a few hours to twenty-two months.

For dissection and roentgen examination a solution of urea and gelatin to which white lead had been added was injected into the arterial system of all the dogs.[16] Before the injection the dog was anesthetized; cannulas were inserted into the femoral artery and vein, and the blood vessels were washed out with saline solution. The washing was completed when a perfectly clear fluid flowed from the outlet of the cannula. The opaque substance already mentioned was then injected into the abdominal aorta. After from twelve to fourteen hours roentgenograms were taken (a front view and a profile view) of the head alone and of the head, neck and shoulders. Autopsy was then performed and the arterial system dissected. As a rule, during the autopsy the brain was taken out and examined by the roentgen rays. In cases in which the dog had died with symptoms of acute bulbar anemia or some kind of accidental disease, the blood vessels were washed out and the injection made immediately after death.

Most of the dogs were puppies, aged from 1 month to 1 year. One dog was about 9 years old. Our experience showed that after simultaneous ligation of the four main arteries about 40 per cent of the dogs died during the first twenty-four hours. Old dogs seldom survived this operation; puppies were more tolerant of ligation of the four arteries than adult dogs. Of the twenty-four dogs operated on, seven (dogs 2, 3, 5, 7, 10, 11 and 17) died with symptoms of acute bulbar anemia during the first twenty-four hours after operation as a result of the ligation of the arteries. Three puppies (dogs 1, 6 and 16) survived the ligation of the arteries but died of distemper. Dogs 12 and 24 died under the anesthetic during operation. The remainder of the dogs died from loss of blood during the washing out of the blood vessels.

16. The solution was made up as follows: gelatin, 120 flakes; urea, 3.375 Gm.; distilled water, 4,500 cc. Lead carbonate (chemically pure) was added gradually, to the amount of about 8 teaspoonfuls for each 500 cc. of the mixture.

Positive and negative conditioned reflexes were established in two dogs (23 and 24) before operation. Work with conditioned reflexes on two other dogs (4 and 8) was begun after the first operation. The last two dogs were first operated on at the age of 2 months and were under observation for two years.

EXPERIMENTAL RESULTS

I. DEVELOPMENT OF COLLATERAL PASSAGES AND CEREBRAL CIRCULATION DURING THE FIRST TWENTY-FOUR HOURS AFTER LIGATION OF THE MAIN ARTERIES

This group of so-called "acute" experiments was carried out on twelve dogs (2, 3, 5, 6, 7, 10, 11, 17, 18, 20, 21 and 22). Simultaneous ligation of four arteries (both common carotid and both vertebral) was performed on six of these dogs. Seven dogs of this group died during the first twenty-four hours after operation with symptoms of acute bulbar anemia. During the autopsy and roentgen examination of these dogs the opaque substance was seen in both the peripheral and the central ends of the tied arteries. Above the ligatures a small amount of opaque substance had entered the main arteries only. On the roentgenogram the muscular and subcutaneous branches were not visible in the upper part of the neck, but they were clearly indicated in the middle and lower parts of the neck. The zone of demarcation, however, was never pronounced. The external carotid arteries and their branches contained a larger amount of the injected substances than the internal carotid arteries. The arteries at the base of the brain and those of the circle of Willis contained a slight amount of the opaque substance. The arteries on the convex surface of the brain were empty. Thus, in the dogs that died with symptoms of acute bulbar anemia after the ligation of four arteries, the cerebral circulation, though greatly restricted, was not completely obstructed. Evidently there was a sufficient number of collateral passages and anastomoses to support for a few hours the activity of the important centers necessary to life.

Dog 18.—This animal was killed five hours after the ligation of both common carotid and both vertebral arteries. Neither symptoms of acute bulbar anemia nor those of any cortical disturbances were observed immediately after the operation. (This dog, unlike the other dogs in this group, could be included in the group of those that survived ligation of the four arteries.) Roentgenograms of the arteries in the neck and brain of this dog are shown in figures 1, 2 and 3. The peripheral parts of both common carotid and both vertebral arteries contained a fair amount of the opaque substance, although less than the central parts of these arteries. The basillar artery and the circle of Willis contained a slight amount. At the base of the brain the main trunk of the middle cerebral artery was clearly indicated. The injected material did not reach the upper surface of the cerebrum and cerebellum. Five hours after the ligation of the four arteries, the following collateral passages and anastomoses had developed: The caudal (inferior) thyroid artery had anastomosed with the cranial superior thyroid artery. Muscular

branches of the vertebral arteries had formed collateral passages with the arteries of the costocervical trunk, viz., the transverse cervical, deep cervical and intercostal superior arteries. The ascending cervical artery from the omocervical trunk had anastomosed with the vertebral, occipital and posterior auricular arteries. The last two arteries had also formed anastomoses directly with the terminal

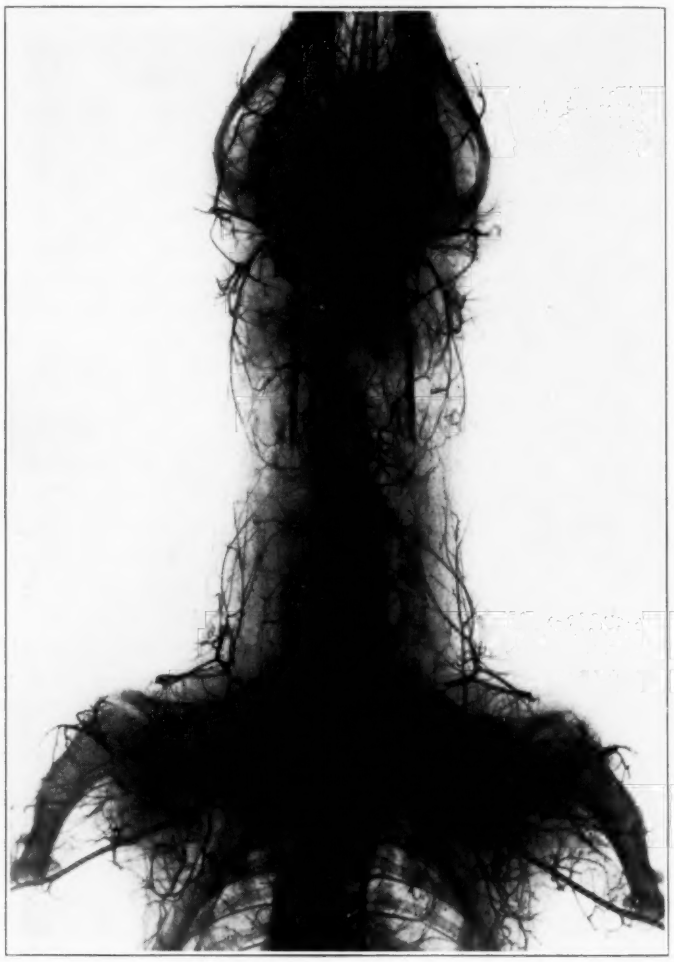

Fig. 1 (dog 18).—Roentgenogram of the blood vessels of the head, neck and shoulders into which an opaque substance was injected; front view. For explanation of this and the other figures see the table and the text.

branches of the vertebral, superior cervical and cranial spinal arteries. The anterior spinal artery at the level of every segment of the spinal cord receives branches from the vertebral arteries in the neck and from the intercostal arteries in the chest. Muscular, cutaneous and subcutaneous anastomoses had developed

Fig. 2 (dog 18).—Profile view.

Fig. 3 (dog 18).—Blood vessels of the brain.

very slightly. The branches of the vertebral arteries and their anastomoses are schematically shown in figure 4.

Dog 20.—Simultaneous ligation of the common carotid, vertebral, internal carotid and occipital arteries on both sides was performed in dog 20. Immediately after the operation the dog became unconscious. The symptoms of acute anemia were not pronounced. The animal was killed four hours after the operation. Figures 5 and 6 show collateral passages and anastomoses in this dog after the ligation of the eight arteries. The arterial system in front of the ligatures was slightly injected; the vertebral arteries cranial to the ligatures contained scarcely any of

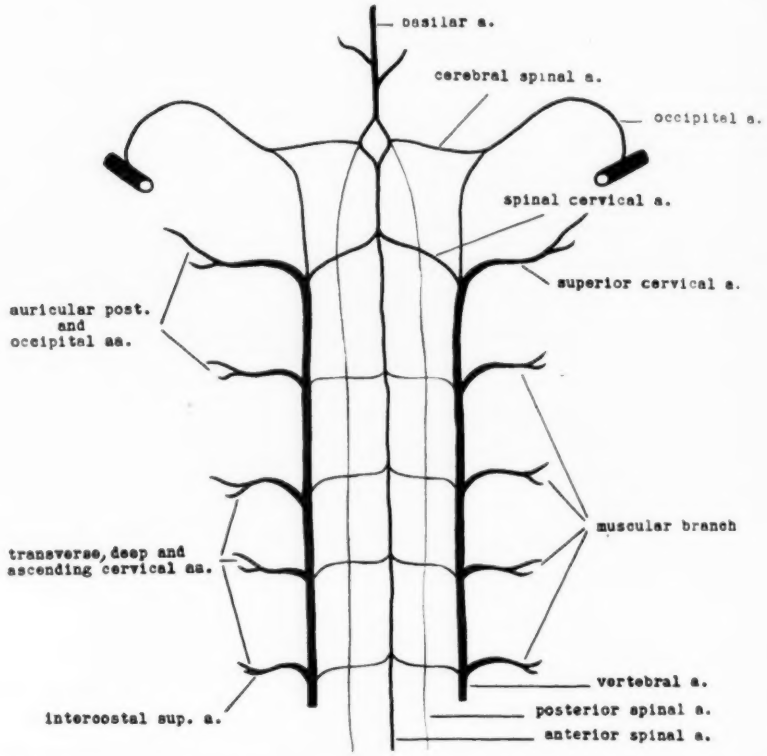

Fig. 4.—Schematic drawing of the distribution of the vertebral arteries and their branches and anastomoses.

the opaque substance. The peripheral parts of the common carotid and the external carotid arteries were better filled with the opaque substance. The internal carotid and basilar arteries and the circulus arteriosus, as well as the main arteries at the base of the brain, also contained a little of the opaque substance. The substance had not penetrated into the arteries of the hemispheres and cerebellum. The anterior spinal artery was slightly injected. Thus, as a result of the ligation of both occipital and both internal carotid arteries restriction of the cerebral circulation was more pronounced than in the case of dog 18 after ligation of only four arteries.

Fig. 5 (dog 20).—Profile view.

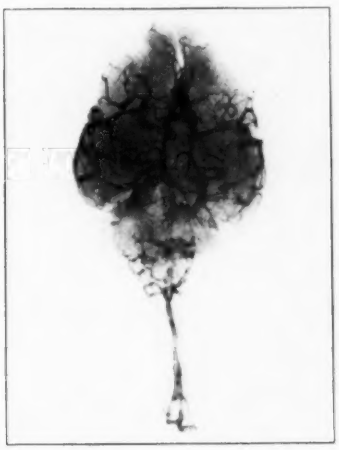

Fig. 6 (dog 20).—Blood vessels of the brain.

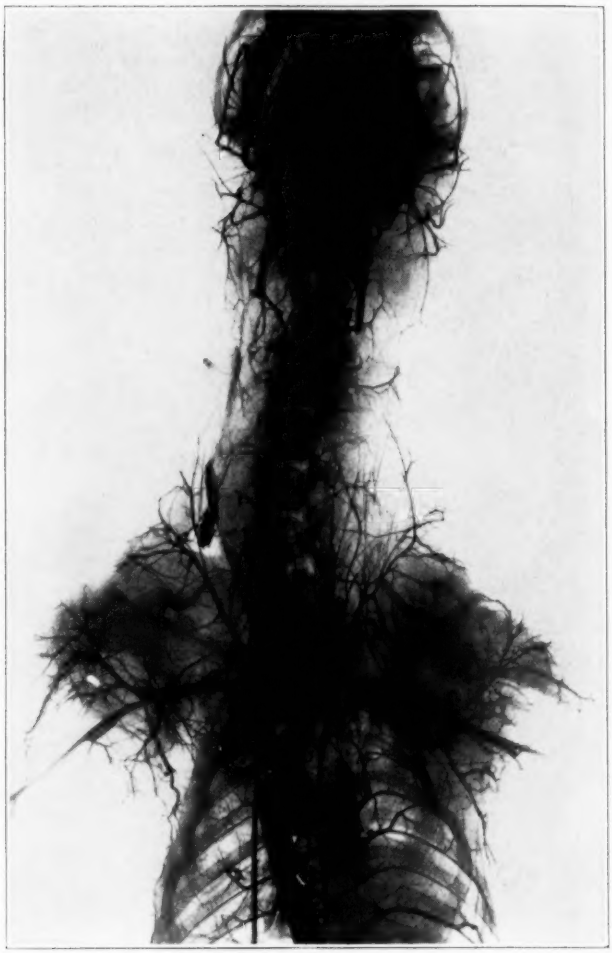

Fig. 7 (dog 21).—Front view.

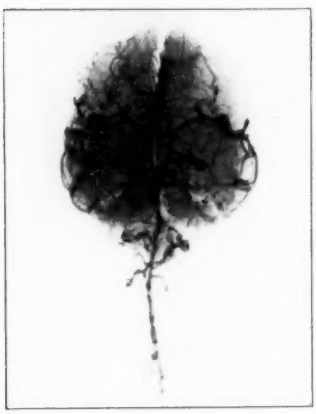

Fig. 8 (dog 21).—Blood vessels of the brain.

This is also due to the fact that in dogs the occipital artery is larger than the internal carotid artery and is important for cerebral circulation. The superior cervical branch of the occipital artery anastomoses with the terminal branch of the vertebral artery. Both arteries unite to give origin to the cerebral spinal artery, which joins the basilar artery. In addition to this, branches from the occipital artery communicate with branches of the ascending and deep cervical arteries (arising

Fig. 9 (dog 22).—Front view.

from the subclavian artery). These anastomoses became enlarged in the muscles of the neck after ligation of both common carotid arteries and formed important collateral passages. The internal carotid artery in dogs does not give out branches until it enters the skull. This artery has an important anastomosis with the internal maxillary artery through the ophthalmic artery.

Thus, four hours after simultaneous ligation of eight arteries, collateral passages developed as follows: 1. The cranial thyroid artery anastomosed with the caudal thyroid artery. 2. The anastomoses between the branches of the vertebral artery and the branches of the omocervical and costocervical trunks were enlarged. 3. The posterior auricular artery anastomosed with the vertebral, deep cervical and ascending cervical arteries.

Dog 21.—Both common carotid and both vertebral arteries, the latter behind, between the first and second cervical vertebrae were tied and cut simultaneously in this animal. After the ligation the dog was in a state of prostration. It did not react to painful stimuli and did not respond to sounds. Symptoms of acute bulbar anemia were slightly manifested. The animal was killed four hours after the operation. All the arteries were slightly injected above the ligatures (figs. 7 and 8). The basilar artery contained scarcely any of the opaque substance. Only the anterior part of the circle of Willis at the point of union with the internal carotid artery was slightly filled with it. The anterior and middle cerebral arteries were also only slightly injected. The numerous small branches of the basilar artery to the pons and medulla were not injected. The arteries on the convex surface of the hemispheres did not contain any of the opaque substance.

Collateral passages had developed very slightly. Both vertebral arteries were excluded from the collateral circulation of the blood by a double ligation. The circulation of blood in the arteries above the ligatures was due to the development of collateral passages between the following arteries: (1) the cranial thyroid artery and the caudal thyroid artery, (2) the occipital and posterior auricular arteries and branches from the omocervical and costocervical trunks and (3) the anterior and posterior spinal arteries and branches of the vertebral and intercostal arteries.

Dog 22.—In the last experiment in this group both common carotid and both vertebral arteries were tied and cut low in the neck; both common carotid arteries were also tied and cut above the origin of the cranial thyroid artery, and both internal and external carotid arteries and both occipital arteries were tied and cut. The parts of the common carotid arteries between the ligatures were excised. A part of each of them, about 2 cm. in length, was left together with the cranial thyroid arteries. All the arteries were tied simultaneously during one operation. After the operation the dog was in a state of great prostration. There was no response to sound, light or painful stimuli. The rectal temperature was 35 C. (95 F.). Respirations (13 a minute) were deep and involved the muscles of the chest. Four hours after the operation the dog was killed. The arteries above the ligature were observed to be injected very slightly; both vertebral arteries and also the branches of the external carotid arteries contained very little of the opaque substance (figs. 9 and 10). The internal carotid arteries were not injected. The circle of Willis was injected very slightly. The middle cerebral artery contained more of the opaque substance than the other cerebral arteries. On the convex surface of the brain only the large arteries were injected. The anterior spinal artery contained the opaque substance only at intervals. Parts of the common carotid arteries left in connection with the cranial thyroid arteries, as well as these arteries, contained the opaque substance. This shows the importance of the cranial thyroid arteries in the development of collateral passages after

double ligation of the common carotid arteries. The aforementioned parts of the common carotid arteries, with the cranial thyroid arteries, represent the connecting link between the caudal thyroid arteries and the posterior auricular arteries.[17] Besides this, branches of the cranial thyroid artery anastomose with the esophageal arteries arising from the thoracic aorta. The large branch from the cranial thyroid artery, viz., the ascending pharyngeal artery, anastomoses with the superior laryngeal artery and with the cervical branch from the occipital artery. The second branch from the cranial thyroid artery, the cricothyroid artery, anastomoses with the ascending cervical artery. There are numerous small branches communicating with the right and left cranial thyroid arteries. This important system of anastomoses enlarges after ligation of both common carotid arteries in the neck.

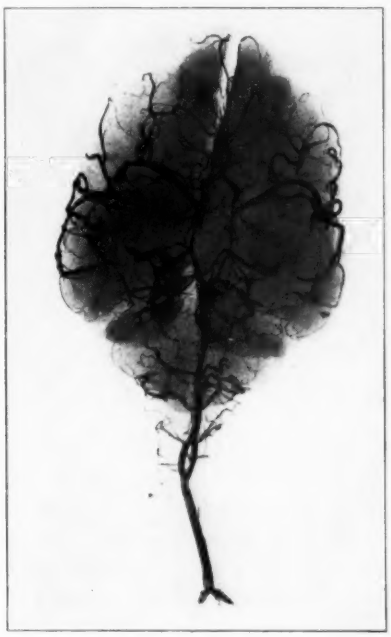

Fig. 10 (dog. 22).—Blood vessels of the brain.

Simultaneous ligation of the ten main arteries supplying the brain did not produce complete occlusion of the cerebral circulation, but it is obvious that under these conditions the circulation of blood in the brain was so restricted that the activity of the vital cerebral centers was greatly impaired. After such ligation, however, the animal may

17. The caudal thyroid arteries in dogs arise from the origin of the common carotid or the subclavian artery (Ellenberger and Baum: Anatomie des Hundes, 1891). Lubomudroff found that the right caudal thyroid artery begins from the innominate artery in 77 per cent of cases and the left caudal thyroid artery from the left subclavian artery in 68.5 per cent.

not immediately succumb. In this case the dog survived for four hours. The continuance of the cerebral circulation was due to the collateral passages and anastomoses between the following arteries: (1) the cranial thyroid arteries and the caudal thyroid, esophageal and ascending cervical arteries; (2) the vertebral arteries and the transverse, deep ascending cervical and posterior auricular arteries; (3) the posterior auricular arteries and the ascending cervical and deep arteries; (4) the anterior and posterior spinal arteries and the spinal branches from the vertebral and intercostal arteries.

II. DEVELOPMENT OF COLLATERAL PASSAGES AND CEREBRAL CIRCULATION WITHIN THE FIRST THIRTY DAYS AFTER LIGATION OF THE MAIN ARTERIES

This group comprised five dogs (1, 9, 11, 16 and 24). In two cases (dogs 1 and 16) simultaneous ligation of four arteries (both common carotid and both vertebral arteries) was performed.

Dog 1.—This animal lived for twenty days after the operation, when it died of distemper. No pronounced changes were observed in the general behavior after operation.

Dog 16.—This animal was operated on in the same manner as dog 1, but after the operation severe cortical disturbances appeared. Immediately after the operation the dog was unconscious and in a state of prostration; the mucous membranes were pale; the pupils were dilated; respiration was quickened, and reaction to painful stimuli was absent. On the second day the dog alternately slept and wandered about the room. It stumbled over every object and stopped before obstacles, being unable to find its way around them. It did not answer to its name, nor did it show any interest in food or drink. However, it ate greedily when the food was put into its mouth and drank automatically when its nose was put into water. It was apparently blind and deaf. The dog was observed during twenty-three days. During this time hearing improved. Five days after the operation the dog reacted to sounds by pricking up its ears; it was not friendly to the experimenter and showed its teeth, growled and bit when touched. Twelve days after the operation trophoneurotic ulcers appeared on the forelegs and hindlegs. The dog died of pneumonia (distemper). The behavior of this dog was similar to that of the dogs with the hemispheres removed described by Goltz [18] (1892) and Zeliony [19] (1911). Hill (1900) observed one dog that also exhibited strong cortical disturbances after ligation of four arteries, but this animal recovered ten days after the operation. During the autopsy and roentgen examination of dog 16 it was noted that the arteries at the base of the brain contained scarcely any of the opaque substance, while the arteries of the hemispheres were empty.

18. Goltz, F.: Der Hund ohne Grosshirn, Arch. f. d. ges. Physiol. **51**:570 1892.

19. Zeliony, G. P.: Dog Without Hemispheres, Proc. Soc. Russian Physicians, St. Petersburg, 1911-1912, pp. 50 and 147.

Figures 11 and 12 show the cerebral arteries of a normal dog and of dog 16, respectively. The anterior and posterior spinal arteries in the latter were developed in the same manner as in the dogs of the first group after ligation of four arteries.

Dog 24.—In this dog both common carotid arteries and the left vertebral artery were tied and cut. Two weeks later the second operation was performed; both

Fig. 11 (normal dog).—Blood vessels of the brain.

Fig. 12 (dog 16).—Blood vessels of the brain.

vertebral arteries were tied and cut at the back of the neck between the first and second cervical vertebrae. This dog was trained by the method of conditioned reflexes (see paper II [20]). Two weeks after the second ligation the third opera-

20. Andreyev, L. A.: Functional Changes in the Brain of the Dog After Reduction of Cerebral Blood Supply: II. Disturbances of the Cortex After Ligation of the Arteries, Arch. Neurol. & Psychiat., to be published.

tion was performed. The right common carotid artery was tied above the origin of the superior thyroid artery. The internal and external carotid arteries and the occipital artery on the right side were tied and cut; the parts of the common carotid arteries between the ligatures were excised. The dog died under the anesthetic, unfortunately, during the operation. Thus, a month elapsed between the first ligation and the death of the animal. The collateral

Fig. 13 (dog 24).—Profile view.

passages and anastomosis that were noted in this dog are shown in figures 13 and 14. The arteries above the ligatures were well injected. A large, tortuous network of arteries was observed in the muscles of the subcutaneous tissue and in the skin. The network of arteries was more developed on the left side than on the right. The part of the right common carotid artery communicating with other arteries by only the cranial thyroid artery was also injected. The arteries at the base of the brain were well injected and were enlarged and tortuous. The large and

medium-sized arteries on the convex surface of the brain contained a fair quantity of the opaque substance. The small arteries of the brain in places were not injected. The anterior spinal artery was enlarged to approximately twice its normal size. The collateral passages between the following arteries were enlarged: 1. The cranial thyroid arteries and the caudal thyroid arteries. The left thyroid artery gave out a strong branch to the right thyroid artery and esophageal arteries. 2. The vertebral arteries and the occipital and posterior auricular arteries. The superior cervical branches of the vertebral arteries were enlarged and formed strong anastomoses with the branches of the occipital and posterior auricular arteries. 3. The arteries from the costocervical and omocervical trunks and the vertebral, occipital and auricular posterior arteries. 4. The transverse cervical artery (from the omocervical trunk) and the dorsal thoracic and scapular circumflex arteries (from the axillary artery), mostly on the left side.

Fig. 14 (dog 24).—Blood vessels of the brain.

Thus, one month after the first ligation the same collateral passages were noted as in the cases in which the dogs were killed a few hours after ligation. The difference was in the extent of the anastomoses, the arteries in the animal that died later being enlarged and tortuous.

III. DEVELOPMENT OF COLLATERAL PASSAGES AND CEREBRAL CIRCULATION AFTER GRADUAL LIGATION OF THE MAIN ARTERIES

The ligation of the arteries of the dogs in this group was performed gradually in different operations. The interval between the operation was from nine days to nineteen months. This group comprised seven dogs (4, 8, 13, 14, 15, 19 and 23). Dogs 4, 8 and 23 were examined after ligation of the arteries by the method of conditioned reflexes (see paper II). The arteries were tied and cut in different

combinations. In dogs 8, 13, 14 and 15 the subclavian artery, as well as other arteries, was tied and cut. Dog 4 survived the five operations; dog 23 survived four. The following arteries were tied and cut in this group of animals: the common carotid artery (double ligation above

Fig. 15 (dog 23).—Profile view.

and below the origin of the cranial thyroid artery); the external and internal carotid arteries; the occipital artery; the vertebral artery (double ligation in the neck, front and back), and the posterior auricular artery (only in dog 4).

Dog 23.—This animal survived for three months after the first ligation. The collateral passages and anastomoses in this dog are shown in figures 15 and 16.

Both common carotid arteries were excised almost entirely; only a small part of these arteries was left at the point of origin of the cranial thyroid artery. Both vertebral arteries were enlarged to almost twice their usual size and were well injected. All the muscular branches of the vertebral arteries were enlarged and tortuous. A direct anastomosis between the superior cervical arteries and the occipital and auricular arteries, as well as the deep ascending arteries, could be seen. The left caudal thyroid artery was enlarged to twice its normal diameter. This artery ascends along the middle line of the cranial thyroid artery. The deep transverse and ascending cervical arteries were enlarged and showed anastomoses with the occipital, posterior auricular and cranial thyroid arteries. The ascending cervical arteries had formed numerous anastomoses in the sternomastoid muscles

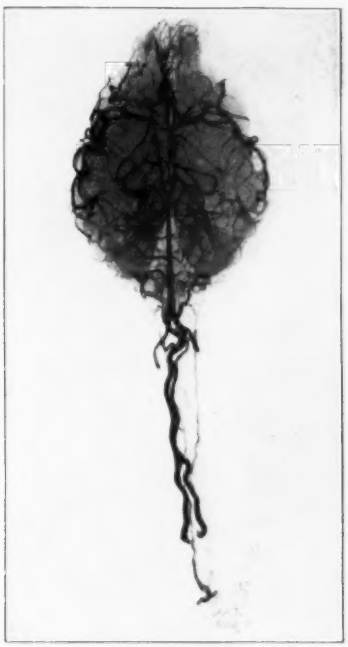

Fig. 16 (dog 23).—Blood vessels of the brain.

with branches of the occipital and posterior auricular arteries. There was one large network of anastomosis at the level of the first and second cervical vertebrae and another at the origin of the larynx. The branches of the cranial thyroid arteries anastomosed with branches of the occipital and lingual arteries. The small branch of the lingual artery, i. e., the hyoid artery, was enlarged and anastomosed with the cricothyroid artery. The anastomosis between the anterior auricular and the posterior auricular artery was enlarged. The middle meningeal and ophthalmic arteries (from the internal maxillary artery) showed a large anastomosis with the internal carotid artery. Branches of the subclavian artery anastomosed with branches of the axillary artery. The superior intercostal artery had an enlarged anastomosis with the other intercostal arteries. The anterior and posterior spinal arteries were enlarged and tortuous. The basilar artery was well injected. All the main arteries

at the base of the brain contained a fair quantity of the opaque substance. The arteries on the convex surface of the brain were only slightly injected, especially on the frontal lobes.

Dog 4.—There was a still more pronounced network of anastomosis in the neck at the base of the skull in this animal, which was killed twenty-two months

Fig. 17 (dog 15).—Front view.

after the first ligation. In this case the posterior auricular artery on the right side was of the same size as the common carotid artery. All the arteries in the neck were enlarged and tortuous. An arterial network was greatly developed in the muscles as well as in the skin and the subcutaneous tissues. The artery following the vagus sympathetic nerve was enlarged. There was enlargement of the arteries in the parotid and submaxillary salivary glands.

If after ligation of both common carotid and both vertebral arteries the subclavian artery was tied and cut (as in dogs 8, 13 and 15), new collateral passages developed, as well as those already mentioned.

Dog 15.—In this case the left subclavian artery was tied and cut (figs. 17 and 18). The esophageal arteries were seen to be enlarged and to have anastomosed

Fig. 18 (dog 15).—Profile view.

with both caudal and both cranial thyroid arteries. An especially strong anastomosis was noted between the superior intercostal artery and the intercostal arteries I to V. The omocervical and costocervical trunks were entirely separated from the subclavian artery by ligation and were injected through the anastomosis. An important anastomosis, which must be particularly remarked, had formed between the subscapular artery (a branch of the axillary artery) and the intercostal arteries.

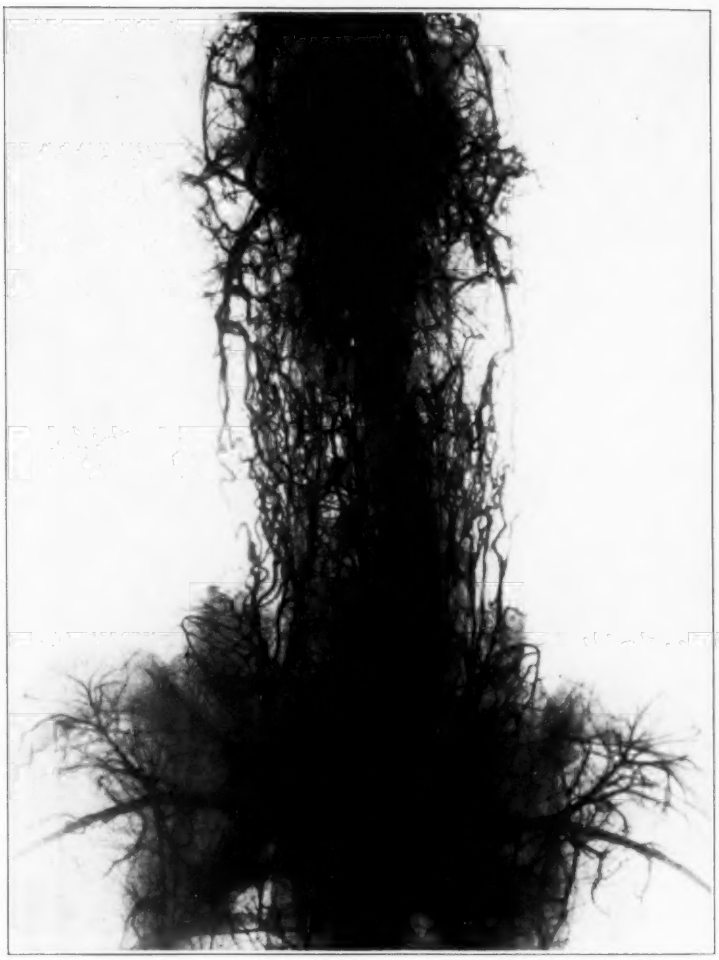

Fig. 19 (dog 4).—Front view.

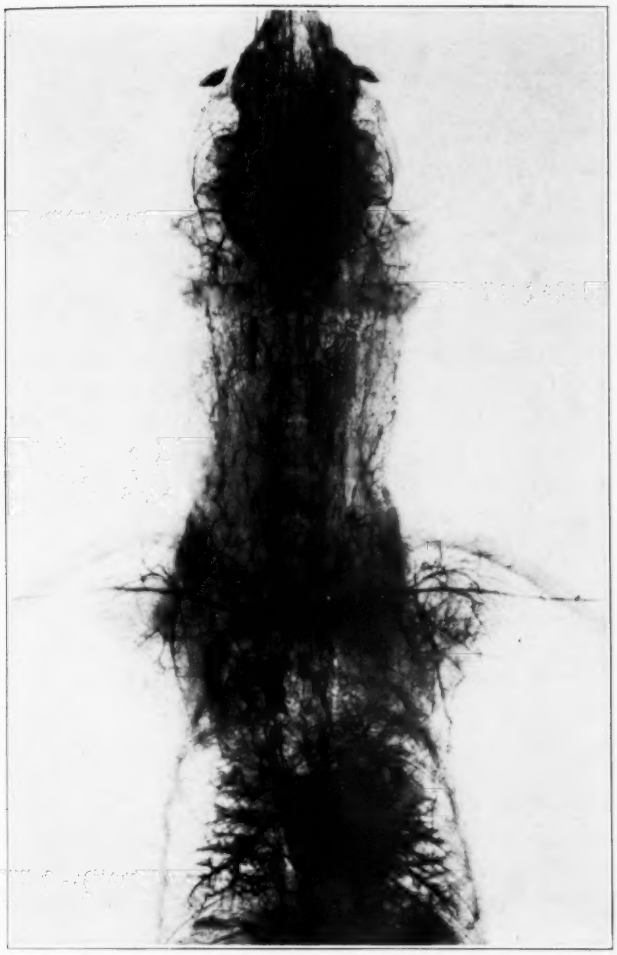

Fig. 20 (dog 8).—Front view.

Fig. 21 (dog 8).—Blood vessels of the brain.

When ligation was performed gradually, as in the case of dog 8, and in addition to ten main arteries supplying the brain the subclavian artery was tied and cut, anastomoses and collateral passages were fairly well developed. The collateral passages and anastomoses in dogs 4 and 8 are shown in figures 19, 20 and 21.

SUMMARY AND CONCLUSIONS

1. When four arteries (both common carotid and both vertebral) were simultaneously ligated in the neck of dogs, about 40 per cent of the animals died within twenty-four hours with symptoms of acute bulbar anemia.

2. The dogs survived ligation of ten arteries supplying the brain if the ligations were performed gradually at intervals of from ten to fourteen days.

3. The development of collateral passages begins immediately after ligation of the arteries and is completed in approximately from four to six weeks. After that a process of enlargement takes place in the collateral passages and anastomoses, which may continue for a year or more.

4. After ligation of both common carotid and both vertebral arteries in the neck, the main collateral passages begin to develop between: (*a*) the caudal thyroid and the cranial thyroid arteries; (*b*) muscular branches of the vertebral artery and the transverse, deep, ascending cervical and superior intercostal arteries, from the costocervical and the omocervical trunks; (*c*) muscular branches of the vertebral artery and the occipital and posterior auricular arteries; (*d*) the anterior and posterior spinal arteries and spinal branches from the vertebral and intercostal arteries; (*e*) the occipital and posterior auricular arteries and the deep cervical and ascending cervical arteries.

5. If in addition to both common carotid and both vertebral arteries the internal and external carotid, the occipital and the posterior auricular arteries are tied, or if an additional ligation of the common carotid arteries above the origin of the cranial thyroid artery is performed, or if the vertebral arteries are tied a second time between the first and second cervical vertebrae, in addition to the collateral passages already mentioned, the following passages are developed: (*a*) The branches of the cranial thyroid artery become the connecting link between the branches of the external carotid artery and the branches of the subclavian arteries and even the thoracic aorta; (*b*) the branches of the internal maxillary artery (i. e., the middle meningeal and ophthalmic arteries) anastomose with the internal carotid artery; (*c*) all the collateral passages in the muscles in and underneath the skin and in other organs are greatly enlarged.

6. If ligation of the subclavian artery is combined with ligation of the common carotid arteries and both vertebral arteries, anastomoses are enlarged between: (*a*) the superior intercostal artery and the other intercostal arteries; (*b*) the transverse cervical and the scapular circumflex arteries; (*c*) the external mammary and the ascending cervical arteries; (*d*) the superficial cervical and the thoracodorsal arteries; (*e*) the scapular circumflex and the transverse cervical arteries.

7. After ligation of four arteries the cerebral circulation may be completely restored, but usually there are symptoms indicating that the nutrition of the brain was more or less impaired.

8. After ligation of more than four arteries the supply of blood to the brain appears to be permanently decreased, and there are symptoms of disordered cerebral function (see paper II).

THE PECULIAR CELLS OF PICK'S DISEASE

THEIR PATHOGENESIS AND DISTRIBUTION IN DISEASE

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In Professor Spielmeyer's laboratory what may be called Pick's cells have from time to time been observed in pathologic states other than Pick's disease. Von Braunmühl [1] and Merritt and Springlova [2] have described Pick's cells in cases of Lissauer's dementia paralytica. It became of interest to know to what extent these cells were to be found apart from this disease entity. From the resulting study a conception of the pathogenesis of these cells was developed. Moreover, the parallel between Pick's cells and axonal chromatolysis (*primäre Reizung*) became apparent.

With Nissl's stain Pick's cells are usually swollen, ballooned-out structures having an oval or globular outline. There is a loss of axial direction and lessened prominence of the cell processes, especially of the apical dendrite. Nissl's bodies disappear or remnants remain at the periphery. The cytoplasm takes on a pale, frosted-glass appearance. The nucleus is displaced to the extreme rim of the cell, usually without alteration. Pigment, if present, is also removed to the periphery.

Alzheimer [3] in an early work divided Pick's cells into three categories on the basis of the observations of sections with Bielschowsky's stain. Von Braunmühl,[4] an exception, has followed the same classification. The representative cell of the first group, variable I (here so designated for convenience and clarity), contains a distinctive, usually globular, homogeneous argentophilic body, often containing lacunae (fig. 1). Neurofibrils are retained to varying degrees or are absent. Of the three variables this is the most numerous in Pick's disease. In variable II the entire cytoplasm is converted into an argentophilic mass, usually homogeneous, though it may be slightly granular. Neurofibrils may be

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From the Deutsche Forschungsanstalt für Psychiatrie, Munich, Germany.

1. von Braunmühl, A.: Synäresis und Entzündung, Ztschr. f. d. ges. Neurol. u. Psychiat. **148**:1, 1933.

2. Merritt, H. Houston, and Springlova, M.: Lissauer's Dementia Paralytica, Arch. Neurol. & Psychiat. **27**:987 (May) 1932.

3. Alzheimer, A.: Ueber eigenartige Krankheitsfälle des späteren Alters, Ztschr. f. d. ges. Neurol. u. Psychiat. **4**:354, 1911.

4. von Braunmühl, A.: Picksche Krankheit; Die Anatomie der Psychosen, in Bumke, O.: Handbuch der Geisteskrankheiten, Berlin, Julius Springer, 1930, vol. 11, pt. 7.

distinguishable in the periphery (fig. 2). Variable III contains a tangled whorl of uniform, delicate fibrils (fig. 3 *A*). This cell is rare in Pick's disease.

Variables I and II of Pick's cells were found in many pathologic states apart from Pick's disease. This is shown in the table. No

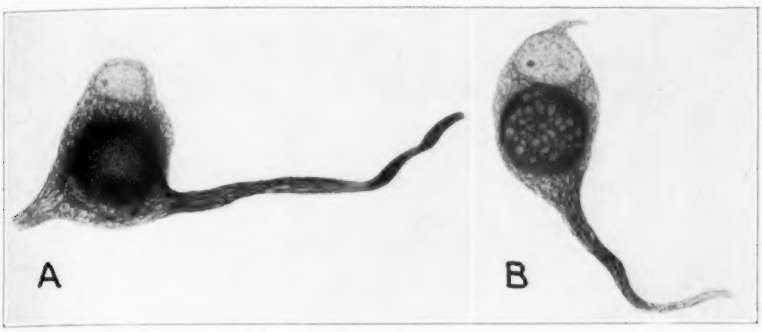

Fig. 1.—*A* illustrates a variable I of Pick's cell containing a round, structureless, homogeneous, argentophilic globule. The displaced nucleus lies in the periphery. A process contrary to the usual picture is evident for a long distance. The cell was noted in a case of juvenile dementia paralytica in a patient aged 17. *B* illustrates a variable I of Pick's cell in which the argentophilic globule contains fine vacuoles. The cell was noted in a case of juvenile dementia paralytica in a patient aged 23. Bielschowsky's stain.

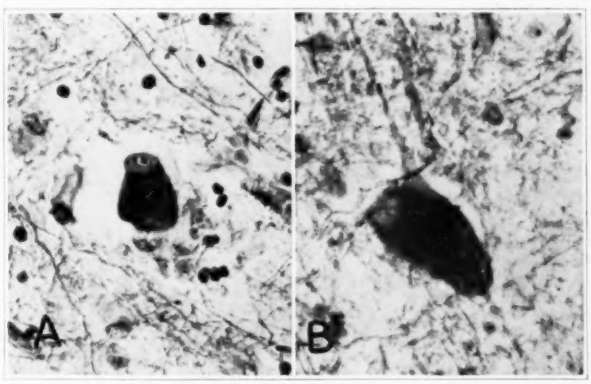

Fig. 2.—*A* is a photomicrograph of a variable II of Pick's cell showing the entire cytoplasm converted into a homogeneous, structureless, argentophilic mass. No processes were evident, and the nucleus lay on the rim of the cell. This was taken from the same section as the cell shown in figure 2. *B* is a photomicrograph of a large variable II cell, the cytoplasm of which is a homogeneous argentophilic mass which does not extend into the processes but is sharply delimited. This was noted in the case of Loeffler in which there was subcortical softening.

attempt was made to classify these cells separately, as the one was inseparably associated with the other.

Observations on Pathologic States Other Than Pick's Disease in Which Pick's Cells Were Noted

Patient	Age, Years	Diagnosis	Pick's Cells			White Matter	Cortex
			Region	Layer	Number		
Rosskam (van Bogaert and Scholz: Ztschr. f. d. ges. Neurol. u. Psychiat. **141**: 510, 1932)	4	Diffuse familial disease of white matter	Precentral	5	Rare	Extensive destruction of myelin and axons	In comparison, slightly involved
Holzapfel (Bodechtel and Guttmann: Ztschr. f. d. ges. Neurol. u. Psychiat. **133**: 601, 1931)	8	Diffuse encephalitis	Frontal; precentral; insula; subiculum	5 and 6	Numerous	Diffuse destruction of myelin and axons; marked progressive gliosis	Slight loss of neurons; glial reaction as in paralysis
Manhard	16	Juvenile dementia paralytica	Frontal	5 and 6	Numerous	Disproportionate degree of destruction; marked progressive gliosis	Beginning status spongioses in third layer
Kreitmeier	17	Juvenile dementia paralytica	Frontal	6	Numerous	Intense progressive subcortical gliosis	Only slight loss of neurons
Gast	22	Disseminated encephalomyelitis	Temporal; frontal	5 and 6	Few	Progressive gliosis	No significant change
Barré (Barré and van Bogaert [5])	23	Concentric familial disease of white matter	Postcentral; frontal; insula; claustrum	5 and 6	Numerous	Localized subcortical progressive gliosis and fibrosis; axonal destruction	Pick's cells found opposite lesions of white matter; no significant change
Doyle	23	Juvenile dementia paralytica	Frontal	3, 5 and 6	Numerous	Disproportionate degree of destruction; marked progressive gliosis; axonal degeneration	Typical changes
Fischer [19]	24	Hallervorden Spatz disease	All cortical preparations; substantia nigra	5 and 6	Numerous	Distinct increase of glia; axons showed terminal balls and clubs; especially in cortex	No significant loss of neurons
Wittman	30	Dementia paralytica	Frontal; insula	6	Few	Progressive gliosis	Typical changes
Jüngel	33	Lissauer's dementia paralytica	Temporal; frontal	5 and 6	Numerous	Progressive gliosis; many fat-laden gitter cells; axonal destruction	Mild changes
Bäuml	33	Lissauer's dementia paralytica	Precentral; postcentral; gyrus hippocampus; frontal; occipital	3, 5 and 6	Numerous	Intense progressive gliosis	Typical changes
Sauter	38	Lissauer's dementia paralytica	Frontal; temporal; precentral; uncus	3, 5 and 6	Numerous	Progressive gliosis	Typical changes

Vester	41	Binswanger's subcortical encephalitis	Frontal; insula; claustrum	5 and 6	Numerous	Frontal; recent extensive subcortical softenings; external capsule; progressive gliosis	Relatively intact
de Stella	42	Lead poisoning with circulatory disturbance	Precentral; postcentral	5 and 6	Few	Cells exist on margins of recent, narrow linear softenings, coursing at an oblique angle to the surface	
Trebs	46	Lissauer's dementia paralytica	Frontal; temporal; parietal	5 and 6	Numerous	Disproportionate degree of destruction; marked progressive gliosis; many fat-laden gitter cells	Typical changes
Meggle	48	Lissauer's dementia paralytica	Temporal; frontal	5 and 6	Few	Disproportionate degree of destruction; marked progressive gliosis	Severe changes of paralysis
Loeffler	48	Arteriosclerosis with softening	Postcentral	3, 5 and 6	Numerous	Recent softening extending to margin of cortex	Without significant change
Mayer	51	Cerebral syphilis	Frontal	5 and 6	Rare	Disproportionate degree of destruction; progressive gliosis	Softening of first and second layers
Grub	51	Glioma	Frontal	5	Rare	Extension of tumor to cortex	Seemingly normal
Steck	65	Metastatic focal encephalitis with softening	Occipital	3, 5 and 6	Numerous	Softening directly beneath cortex	Seemingly normal
Dobler	65	Circulatory disturbance	Uncus	5 and 6	Few	Marked gliosis	Seemingly normal
Glass	66	Softening of brain; cachexia of malignant process	Occipital; temporal	5 and 6	Rare	Marked subcortical gliosis; inanition atrophy (?)	Seemingly normal
Winklmaier	67	Binswanger's subcortical encephalitis	Occipital; frontal	5 and 6	Few	Extension of softening to cortex	
				6	Rare	Progressive subcortical gliosis	Localized cell loss
Feiner	76	Arteriosclerosis with softening	Gyrus hippocampus; gyrus fusiformis	5 and 6	Few	Progressive subcortical gliosis	Slight cell loss
Wagatha	76	Arteriosclerosis with softening	Parietal	5	Rare	Extension of softening to cortex in limited area	Seemingly normal
Hofner	78	Arteriosclerosis with softening	Insula; claustrum	3, 5 and 6	Few	Progressive gliosis in external capsule and capsula extrema	Gliosis in claustrum; insula, seemingly normal
Höhl	87	Arteriosclerosis with softening	Frontal; insula; claustrum	5 and 6	Few	Disproportionate degree of destruction; progressive gliosis	Slight cell loss

From the table it is apparent that these cells may occur independent of any age factor. They were found in every age group from 4 to 87 years. Nor seemingly is there any correlation with etiologic factors. They may occur in frank infectious diseases, such as syphilis, in heredodegenerative diseases, such as diffuse familial disease of the white matter, in diseases with disturbed cerebral circulation and in the presence of tumors.

Certain conditions occurred repeatedly in the various cases in which these cells were found. Most impressive was the invariable presence of pathologic changes in the white matter. The pathologic change took the form either of progressive gliosis or of a break in the continuity of the tissue (table). In the instances of gliosis of the white matter the glial elements were hypertrophic and hyperplastic. Usually the gliosis was diffuse in the white matter involved. However, in three cases it was limited to the subcortex. In the case of Barré and van Bogaert [5] pathologic changes consisting of progressive gliosis and fibrosis existed, in three different cerebral preparations, only under fractions of the cortex, as for example, at the base of a sulcus. Only in the cortex overlying this delimited change of the white matter were variables I and II found.

The break in the continuity of the white matter was brought about by softening of an arteriosclerotic origin or, in one instance, by a tumor. Here, also, the location of the pathologic change was significant. Variables I and II were found when such interruptions in continuity of the tissue occurred immediately beneath the cortex. This was true in the two cases of "Binswanger's subcortical encephalitis." In four patients (Loeffler, Steck, Wagatha and Winklmaier) the softening had destroyed most of the U-fibers of Meynert but had left the sixth layer essentially intact. The tumor of patient Grub had reached the subcortex.

In contrast with the condition in the white matter, no constant cortical changes were observed in association with variables I and II. Indeed, the cortex could otherwise be free from significant pathologic change (table). Furthermore, satellites were indifferent to these altered neurons; they provoked no glial reactions whatsoever. Satellites, if anything, were fewer than normally.

As to distribution, variables I and II were observed roughly in all regions of the cerebral cortex. In addition, they were found in the claustrum in four instances and in the substantia nigra in one instance. Within the cortex they existed principally in the fifth and sixth layers and only exceptionally in the third. Neighboring cells were commonly not so transformed. Rather, these cells tended to be isolated.

5. Barré, J. A., and van Bogaert, Ludo: Contribution à la dissociation anatomique et clinique des leuco-encéphalites subaigües: Le type concentrique de Baló, Rev. neurol. **1**:547 (April) 1933.

Variable III was not found in association with variables I and II. From this observation arose a doubt as to the correctness of classifying this cell with Pick's cells. Alzheimer,[3] when describing these cells, stressed their rarity and similarity to the early forms of Alzheimer's fibrillary changes. Fényes[6] reported finding this cell in certain nuclei of the brain stem and basal ganglia in a case of postencephalitic parkinsonism. He was impressed by the whorl formation of the fibrils within the ballooned-out cells but unhesitatingly regarded it as a variety of Alzheimer's fibrillary changes. My experience was similar to that of Fényes. In six cases of chronic epidemic encephalitis this cell type was found in the brain stem and especially readily in the midbrain. In neighboring cells characteristic forms of Alzheimer's fibrillary changes were found in several instances (fig. 3). This association was also met with in the presubiculum of the cornu ammonis in two persons of

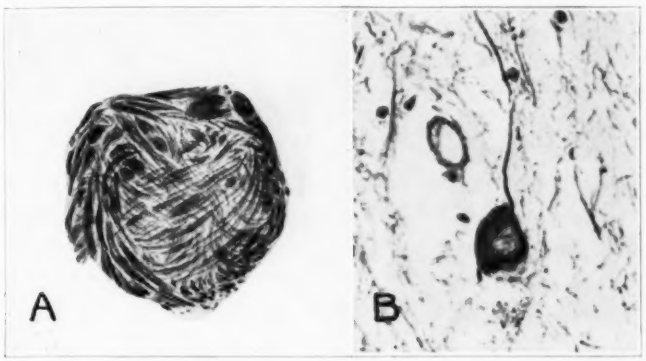

Fig. 3.—*A* illustrates a large cell with a fibrillary whorl formation from the gray matter about the aqueduct of Sylvius in a patient 29 years of age with postencephalitis. *B* is a photomicrograph of a neighboring cell showing classic Alzheimer fibrillary changes. Bielschowsky's stain.

advanced age. In my opinion, then, the term Pick's cells should be limited to variables I and II.

COMMENT

A significant factor in the pathogenesis of variables I and II of Pick's cells is suggested from the observation that the presence of these cells is inseparable from pathologic changes in the white matter. Axons are spared from destruction in lesions of the white matter only in multiple sclerosis and in certain cases in Schilder's disease. In each case listed in the table it is possible to postulate that certain of the axons were subject to alteration. In five of the cases actual axonal destruc-

6. Fényes, Istran: Alzheimersche Fibrillenveränderung im Hirnstamm einer 28 jährigen Postencephalitikerin, Arch. f. Psychiat. **96**:700, 1932.

tion was observed by other workers, as revealed in the reports of cases from the Forschungsanstalt. Axonal destruction in cases of softening is a foregone conclusion. In Lissauer's dementia paralytica, Merritt and Springlova [2] described a loss of white matter that is independent of the cortical pathologic changes. In seven of their eight cases, ballooned-out cells (*Zellblähungen*) similar to those under discussion were found. Müller and Bielschowsky [7] reported pathologic changes in the white matter unrelated to cortical pathologic change in dementia paralytica. Müller [7a] found ballooned-out cells in his case. It would seem, then, that some alteration in the axon preceded the development of variables I and II. That the cortex may be normal apart from the presence of Pick's cells may be construed as support for the rôle of the axon in the development of these cells.

However, indiscriminate axonal alteration does not result in the production of Pick's cells. Certain conditions must be fulfilled. Two of these conditions were evident from this study. Thus, the site of axonal injury must be near the cell of origin. Pick's cells were found where areas of softening approached the cortex. This condition was also recognizable in the case reported by Barré and van Bogaert [5] and may be inferred in the cases of subcortical gliosis.

Then, too, the axonal alteration must have been of recent consummation. Pick's cells were not found in quiescent, repaired states of the white matter in which an equilibrium had been reached but were present rather in states in which there was evidence of flux as manifest by glia cells in progressive stages. When softening brought about the axonal alteration this condition was also in evidence.

As to the pathogenesis of these cells, Richter [8] was of the opinion that as a result of the swelling the previously unstained plasma stained with Bielschowsky's method. Neurofibrils were pushed asunder by the swollen plasma. Schneider [9] believed that transitory products of degeneration (*Abbau*) became stainable with silver in certain phases of their development. Urechia [10] recognized some transformation of coagulation of the protoplasm. According to von Braunmühl's [11]

7. (*a*) Müller, G.: Progressive Paralyse mit starker Marksklerose, Ztschr. f. d. ges. Neurol. u. Psychiat. **133**:620, 1931. (*b*) Bielschowsky, Max: Ueber Markfleckenbildung und spongiösen Schichtenschwund in der Hirnrinde der Paralytiker, J. f. Psychol. u. Neurol. **25**:72, 1919.

8. Richter, Hugo: Eine besondere Art von Stirnhirnschwund mit Verblödung, Ztschr. f. d. ges. Neurol. u. Psychiat. **38**:127, 1918.

9. Schneider, Carl: Ueber Picksche Krankheit, Monatschr. f. Psychiat. u. Neurol. **65**:230, 1927.

10. Urechia, quoted by von Braunmühl.[11]

11. von Braunmühl, A.: Kolloidchemische Betrachtungsweise seniler und präseniler Gewebsveränderungen, Ztschr. f. d. ges. Neurol. u. Psychiat. **142**:1, 1932.

ingenious theory, the argentophilic material is genetically related to the particles composing the neurofibrils. These particles, as a result of a disturbance in the colloid equilibrium of the cell, lose the factors giving them direction and arrangement in the cell. Then, with the action of the law of small surfaces, these free bodies form a solid globule. In the process of this formation, however, they imbibe water and swell. The factors that bring about the original loss in direction of the particles composing the neurofibrils remain unknown. Any of these theories may be right. However, before such transformation occurs in the cell it is my belief that there must be axonal alteration.

In the face of the proposed pathogenic factor for variables I and II, a parallel between these cells and axonal chromatolysis (*primäre Reizung*) is suggested. Onari and Spatz,[12] Merritt and Springlova,[2] von Braunmühl [11] and Schneider [9] recognized a relationship between Pick's cells and axonal chromatolysis. Schneider [13] demonstrated Betz cells undergoing axonal chromatolysis in one of his cases of Pick's disease. Von Braunmühl [11] remarked that the comparison between these two cell types may be carried further when one recalls the swelling of axons to be observed in Pick's disease and evaluates this swelling as a primary change. The parallel is, I believe, more pronounced. The nucleus in both reaction types commonly evidences no degenerative phenomena. Glia cells are inert to axonal chromatolysis [14] and to variables I and II. Fat pigment and remaining neurofibrils are in both dragged to the periphery of the cell. Fuchsinophilic granules were more prominent in the Pick cells in the case of Loeffler than in other neurons. Spatz [15] made this observation in a case of axonal chromatolysis. The cytoplasmic transformation of the two types does not in itself result in death of the cell. Similar deviations from the usual form may occur. Thus, Peter [14] described great enlargement of processes of cells undergoing axonal chromatolysis; the enlargement is stainable for long distances, resembles a piece of tubing and produces peripheral displacement of retained neurofibrils. These cells, as seen in Bielschowsky preparations from Peter's case, are without appreciable morphologic difference from those in two of my cases (Vester, Winklmaier; fig. 4).

12. Onari, K., and Spatz, H.: Anatomische Beiträge zur Lehre von der Pickschen umschriebenen Grosshirnrindenatrophie, Ztschr. f. d. ges. Neurol. u. Psychiat. **101**:470, 1926.

13. Schneider, Carl: Weitere Beiträge zur Lehre von der Pickschen Krankheit, Ztschr. f. d. ges. Neurol. u. Psychiat. **120**:341, 1929.

14. Peter, Cuno: Beitrag zur Klinik und pathologischen Anatomie der hereditären Nervenkrankheiten, Ztschr. f. d. ges. Neurol. u. Psychiat. **108**:543, 1927.

15. Spatz, Hugo: Ueber degenerative und reparatorische Vorgänge nach experimentellen Verletzungen des Rückenmarks, Ztschr. f. d. ges. Neurol. u. Psychiat. **58**:327, 1920.

Moreover, it is to be recalled that a relationship exists between the presence of variables I and II and the proximity of the pathologic change of the fibers to these cells. This applies also to axonal chromatolysis. Spatz [15] observed that such a reaction occurred more constantly if the site of the experimental cutting of the axon was near the cell of origin.

In addition, it is noteworthy that in certain sections in which variables I and II existed there were certain cells which, with Bielschowky's stain, were indistinguishable from cells with axonal chromatolysis. In one precentral section (patient Bäuml) there were seen within the extent of a low power microscopic field a Betz cell evidencing axonal chromatolysis and two smaller cells with the typical appearance of variable I (fig. 5). These two cell types, the Pick cell and axonal chromatolysis, may occur under seemingly identical pathogenic conditions.

Fig. 4.—A photomicrograph of a cell which may be classified either as a Pick cell or as a cell showing axonal chromatolysis.

But, whatever parallel there may be, it would seem to be nullified on contemplation of the distinctiveness with the Bielschowsky stain of an argentophilic globule in a variable I cell and the described crumbled, granular contents of a cell with axonal chromatolysis. However, Spatz [15] spoke of the development of a foreign-body mass (*fremdkörperartigen Masse*) in experimentally produced axonal chromatolysis. In preparations from the case reported by Peter,[14] in which there was practically universal conversion of cells of the brain stem into axonal chromatolysis, it is possible to find within the smaller cells, as in the nucleus arcuatus, the nucleus paramedianus dorsalis, the nucleus funiculi gracilis and the nucleus triangularis dorsalis, a definite argentophilic globule (Bielschowsky's stain) identical with those in Pick's disease (fig. 6). Von Braunmühl's basis of differentiation between these cell types, that is, the argentophilic globule wherein a degenerative momentum is in the

foreground, does not seem sufficient. The distinction between variable I on the one hand and axonal chromatolysis on the other becomes increasingly hazy, the parallel more pronounced.

Ramón y Cajal and Miskolczy [16] experimentally sectioned the white matter of the cerebral cortex and reported the resulting tissue reaction.

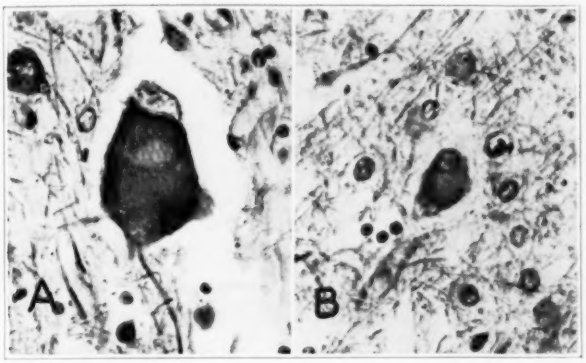

Fig. 5.—*A* is a photomicrograph of a Betz cell in a state of axonal chromatolysis with a granular, crumbly argentophilic cytoplasm. *B* is one of two Pick cells that were seen within the same low power field as the cell in *A*. These cells were noted in the case of a patient (Bäuml) with dementia paralytica with sclerosis of the white matter. Bielschowsky's stain.

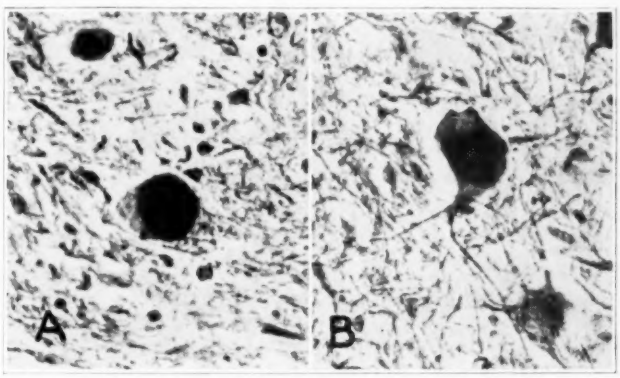

Fig. 6.—Photomicrographs of cells found in Peter's case in which the majority of the neurons have been described as having been in a state of axonal chromatolysis (primäre Reizung). Distinct argentophilic globules are evident. *A* is a section from the nucleus of Goll, and *B*, one from the nucleus arcuatus. Bielschowsky's stain.

16. (*a*) Ramón y Cajal, S.: Degeneration and Regeneration of the Nervous System, New York, Oxford University Press, 1928, vol. 2. (*b*) Miskolczy, Desiderius: Ueber die Frühveränderungen der Pyramidenzellen nach experimentellen Rindenverletzungen, Trav. du lab. de recherches biol. de l'Univ. de Madrid **23**:135, 1925.

No cells resembling variables I and II were described. However, a comparison between the pathologic change so produced and that existent in the white matter in the cases listed in the accompanying table seems difficult. Miskolczy, in a personal conversation, expressed the same opinion and pointed out that his observations were carried out over a short period and that severe circulatory disturbances of the cortex occurred.

Why a cell with an altered axon assumes the form of variable I or II of the Pick cell or of axonal chromatolysis is not clear. It may depend on the inherent morphology of the cell, the site and intensity of the axonal alteration and a time element.

As to inherent morphology, Alzheimer [3] remarked that variable I cells are transformations of the smaller pyramidal cells. It was commonly the smaller pyramidal cells that showed this alteration in the cases listed in the table. Argentophilic globules were found in the smaller cells of the brain stem in Peter's case [14] in which almost universal axonal chromatolysis was seen. On the other hand, classic axonal chromatolysis has been described as occurring only in the large cells of the brain.[17]

As to the site and intensity of the axonal alteration, it has already been indicated that the site of the axonal lesion is significant in the production of variables I and II. Nissl [18] and Spatz [15] have noted that the nearer to the cell of origin the axon is cut, the greater assurance there is of producing axonal chromatolysis. They also found that the intensity of the axonal lesion modifies the morphology of the cell of origin. Axonal chromatolysis is more intense following the tearing out of a peripheral nerve than following clean sectioning with a knife.

As to the time element, variable II cells were observed to be more prominent in the less atrophic areas in Pick's disease and variable I in the more atrophic regions. In one case of this disease (patient Schaiver) variable II was found almost exclusively in the slightly atrophic regions, whereas variable I predominated in the frontal cortex with status spongiosus. In the case of Fischer [19] variable I cells were more numerous than in any other case listed in the table. The clinical duration in this instance was fourteen years. In no other case was there so lengthy a duration.

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17. Spielmeyer, W.: Histopathologie des Nervensystems, Berlin, Julius Springer, 1922.

18. Nissl, F.: Ueber experimentell erzeugte Veränderungen an den Vorderhornzellen des Rückenmarks bei Kaninchen, Allg. Ztschr. f. Psychiat. **48**:675, 1892; Ueber die Veränderungen der Ganglienzellen am Facialiskern des Kaninchens nach Ausreissung der Nerven, ibid. **48**:197, 1892.

19. Fischer, cited by Helfand, Max: Mitteilung eines Falles von Hallervorden-Spatzscher Krankheit, Ztschr. f. d. ges. Neurol. u. Psychiat. **143**:794, 1933.

CONCLUSIONS

Pick's cells are redefined.

Pick's cells are not dependent on the senium or on specific etiologic agents for their development.

A factor seemingly in the pathogenesis of these cells is axonal alteration which is of recent development and located in the vicinity of the cell of origin.

The parallel between Pick's cells and axonal chromatolysis is emphasized.

HEMIPLEGIA WITH THE LEG IN FLEXION

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AND

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Walshe [1] has gone far to explain the mechanism of rigidity appearing in man after injury of the pyramidal tracts, in terms of recent neurophysiologic data. He expressed the belief that the hypertonus is equivalent to that following partial decerebration in laboratory animals and is due to freeing of reflexes of the midbrain from normal control by higher centers. The rigidity that develops after recovery from a cerebrovascular accident involving the corticospinal fibers in the internal capsule is commonly distributed in a stereotyped pattern. The increased tone in the arm is maximal in the flexors of the wrist and fingers, the flexors and pronators of the forearm and the adductors of the upper arm; the attitude of the arm is primarily one of flexion. In the leg the hypertonus is predominate in the flexors of the foot and toes, in the extensors of the knee and in the adductors of the thigh; the position of the leg is one of extension.

The typical hemiplegic position of the extremities is in many ways ideal for the patient who is ambulant. The adduction of the arm and partial flexion at the elbow serve to place the extremity close to the chest out of harm. The leg is held firmly as a prop owing to the tonus of the extensors of the knee. It supports the body well, and there is usually enough power of movement remaining so that the leg may be circumducted and advanced for locomotion.

Although this is the typical arrangement of tone in ambulant patients, in many patients the distribution of tone by no means conforms to this pattern; divergent forms have already been reported in the literature. Walshe has consistently maintained that tone in the extremities of the hemiplegic patient always conforms to the pattern previously outlined; there have usually been good grounds for this criticism.

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1. Walshe, F. M. R.: Physiological Analysis of Some Clinically Observed Disorders of Movement, Lancet **1**:963, 1929.

In 1920, Marie and Foix [2] described the case of a woman aged 70 with paraplegia with the legs in flexion which the authors believed was caused by lesions in the forebrain. The patient showed exaggeration of responses to pain stimuli in the legs and diminution of the tendon reflexes. There was great intellectual enfeeblement with spasmodic laughter. Study of the brain showed progressive subependymal necrosis with involvement of the projection fibers from the paracentral lobules of the cortex.

Alajouanine [3] in 1923 reported a new case which he studied clinically and pathologically. The patient, a woman aged 62, had severe mental changes. There was difficulty in swallowing but no aphasia. Dysarthria and spasmodic laughing and crying were present. The abnormalities developed gradually until finally the patient was unable to walk and was confined to bed. Gradually the legs assumed a posture of semiflexion. There were no local changes in the knee joints, but movement was inhibited by spasticity. Movements of the arms were weak, but the deep reflexes were normal. The abdominal reflexes were abolished. The Babinski response was extremely active and could be elicited even by stimuli applied to the abdomen. There were no abnormalities of sensation. Examination of the brain revealed widespread lacunar degeneration around the arteries. The gray matter of the corpus striatum showed atrophy. The motor projection fibers from the paracentral lobules were involved in the degeneration.

Walshe [4] (1923) objected to the conclusions that these cases of paraplegia in flexion were due to lesions of the forebrain because of the widespread vascular changes. Although the authors stated that no abnormalities were present in the brain stem or spinal cord, Walshe believed that such abnormalities might easily have been overlooked. He felt that there was no justification for abandoning the hypothesis that paraplegia in flexion is dependent on a severe lesion in the spinal cord usually causing complete physiologic transection.

Alajouanine reported incompletely other cases of even more interest in connection with the present problem. One patient, aged 60, with aphasia and hemiplegia of ten years' duration had flexor contracture of the hemiplegic leg. The flexion occurred immediately after the vascular accident. Another person, aged 42, had hemiplegia associated with syphilis and was kept in bed for several weeks after the accident. Ten months after the hemiplegia appeared the leg assumed a flexed

2. Marie, P., and Foix, C.: Paraplégie en flexion d'origine cérébrale par nécrose sous-épendymaire progressive, Rev. neurol. **36**:1, 1920.

3. Alajouanine, T.: Sur un type de paraplégie en flexion d'origine cérébrale avec exagération de l'automatisme médullaire, Paris, Gaston Doin, 1923.

4. Walshe, F. M. R.: Is Babinski's Paraplegia in Flexion Ever Produced by Cerebral Lesions? M. Science **8**:229, 1923.

position. In a third patient, who had hemiplegia at the age of 48, there was a progressive tendency for the leg to assume a flexed position. In all these cases the reflexes of defense were very active. In other patients with lesions of the pyramidal tract combined with parkinsonian rigidity following encephalitis the legs were held in flexion by contracture.

Vincent, Krebs and Chavany [5] (1925) reported two cases of hemiplegia with the leg in flexion; both occurred in elderly persons who were demented. There was severe pain in the paralyzed extremities, which was increased by all cutaneous stimuli and passive manipulation. Both legs were flexed, but the flexion was more marked on the hemiplegic side. In one there was an area of softening in the left hemisphere involving the internal capsule, putamen, globus pallidus and lateral nucleus of the thalamus, and in the other there was softening of the left parietal lobe which extended into the adjacent white matter. Walshe [6] (1925) pointed out the resemblance of the condition in these cases to the thalamic syndrome described by Head and Holmes. The persistent flexion of the lower limbs was regarded by the latter observers as a response to the hyperalgesia.

We have observed fourteen cases of hemiplegia with the leg in flexion; the frequency of such cases in a hospital for chronic diseases is indicated by the fact that they were discovered during the examination of one hundred and fourteen hemiplegic patients. The great majority of the patients were senile and had diffuse vascular lesions; the same objection could therefore be raised as in the case of previous reports that the damage was diffuse in the brain and cord. Some patients, however, were young when the injury occurred. In these cases one could be reasonably certain that the abnormality was confined to the forebrain, and these are described in detail.

REPORT OF CASES

CASE 1.—N. B., a Negro 42 years of age in 1934—was admitted to the hospital on Oct. 6, 1927. On October 4, while at home, he suddenly became unconscious; on awakening he could not use his right arm or leg and could not talk. He was right-handed. Examination revealed facial asymmetry; the mouth was drawn to the left. All deep reflexes on the right were hyperactive; there were a positive Oppenheim reflex and ankle clonus. The right side of the body was hyperesthetic; even a touch with cotton-wool was unpleasant. When the patient was first examined the right leg was markedly flexed at the knee and ankle. Study of the cerebrospinal fluid showed 35 cells, all of which were lymphocytes. The Wassermann reaction was positive in both the blood and the spinal fluid.

5. Vincent, Krebs and Chavany: Pseudoparaplégie en flexion par lésion cérébrale unilatérale, Rev. neurol. **1**:337, 1925.

6. Walshe, F. M. R.: Review of Article by Vincent, Krebs and Chavany, M. Science **12**:288, 1925.

Antisyphilitic treatment was instituted. The right leg remained in flexion at the hip and knee and could not be used in walking. Accordingly, a traction apparatus was placed on the foot, and the extremity was extended. Although it was brought into normal position, the leg at once became flexed and remained in this posture when the weight was removed. During the following five years the patient was in good general health. He sat all day in a wheel-chair and took an active interest in affairs around him. He had a rather large vocabulary, although he was still markedly aphasic. Comprehension was fair, and he was cooperative.

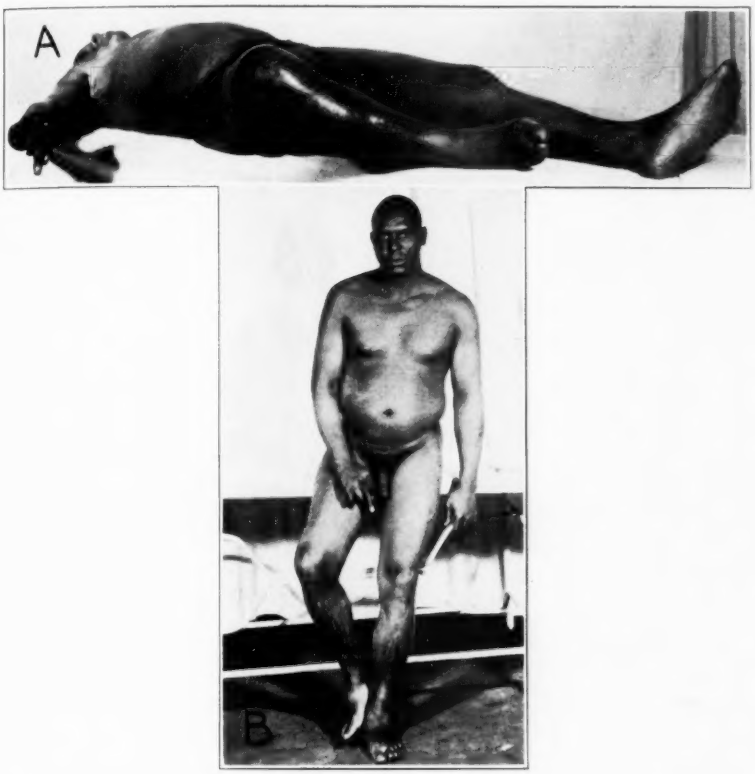

Fig. 1 (case 1).—This patient shows hemiplegia with flexion of the leg at the hip and knee and external rotation at the hip. It was impossible for him to place the foot on the floor. The arm is extended at the elbow.

Examination on Dec. 3, 1934, revealed a well nourished Negro. He could stand against a support, balanced on the left leg, but the right leg was flexed so greatly that the foot could not be placed on the ground (fig. 1 *B*). There were external rotation of the left leg at the hip, flexion at the hip and knee and plantar flexion of the ankle. The foot was internally rotated. The arm was in an unusual position for the condition, in that it was almost completely extended at the elbow (fig. 1). The arm was adducted. The thumb and the index and middle fingers were extended; the ring finger and little finger were flexed.

The patient was highly emotional, expressed himself with particular difficulty during examination and was unable to carry out simple commands, for example, to put the left finger on the nose. There was right hemianopia. The facial folds were less marked on the right, and facial movements were stronger on the left than on the right. The tongue was protruded in the midline. There was marked longitudinal curving of the nails on the hemiplegic side, which was not present on the normal side. A positive Hoffmann reflex was elicited from the index and middle fingers. There was well sustained wrist clonus. The abdominal reflexes were obtained on both sides but became exhausted easily on the right. Stimulation of the paralyzed side of the abdomen caused a response on the sound side. The cremasteric reflex was less active on the right than on the left. Ankle clonus was well sustained. Stimulation of the sole of the foot caused the leg further to be strongly flexed at all joints, but no dorsiflexion of the great toe or fanning of the other toes was seen.

There was considerable spontaneous pain on the hemiplegic side of the body. Stimulation with a pin always caused a sharper sensation on the normal side; the objective response, on the other hand, was always more marked on the paralyzed side. Over this area the slightest touch caused marked motor response and remonstrance, whereas pinprick was perceived on the normal side with equanimity. It seemed, therefore, that pinprick and any sensory stimulus, although perceived better on the normal side, caused a more disagreeable sensation on the hemiplegic side.

The so-called associated movements were somewhat stereotyped in this case, no matter what type of stimulus was used to elicit them; nevertheless, because of slight differences, they will be given in detail. Extension of the neck against pressure caused slight flexion of the hemiplegic arm and marked flexion of the leg; the the same result was obtained on flexion of the neck. Rotation of the head with the chin toward the hemiplegic side produced flexion of the arm with internal rotation of the abnormal leg and adduction of the foot. There was little response when the chin was turned to the normal side; at times there was a tendency to extension of the hemiplegic leg. If the normal arm was held extended at the elbow against pressure the hemiplegic arm and leg were flexed, the flexion of the leg beginning at the ankle. Flexion of the normal arm against pressure caused the hemiplegic arm to flex and adduct and the leg to flex at all joints. A strong grip of the normal hand produced internal rotation of the leg and dorsiflexion of the hemiplegic ankle. Flexion of the normal knee against pressure caused flexion and external rotation of the abnormal leg but no movement of the arm. Similarly, extension of the normal knee caused flexion and external rotation of the abnormal leg.

Other types of stimuli induced flexion of the hemiplegic leg. Stimulation of the lateral wall of the chest on the right side or of the inner aspect of the hemiplegic arm with the finger or a pin caused flexion of the leg. It may be concluded, then, that with almost all types of stimuli which produce associative reactions there was a tendency to further flexion of the hemiplegic leg.

By the use of a traction apparatus the leg was readily extended. It always became flexed on removal of the weight. The patient's leg was held extended by a plaster cast for two weeks, but at once assumed its former position when the cast was removed.

Case 2.—R. W., a Negro aged 46 in 1934, was well until March 1926, when he was found unconscious; when roused he could not speak intelligently or stand without assistance. Before admission to the hospital convulsive seizures occurred

at twenty minute intervals. The eyes were first drawn to the right, and twitching of the right side of the upper lip appeared, the movements spreading to other facial muscles. Within twenty-four hours the attacks became more generalized, extending to the right arm and leg and, finally, over the body. The reflexes were hyperactive and there was ankle clonus on the right. Ophthalmoscopic examination showed distention of the retinal veins and haziness of the margins of the left disk. There was right homonymous hemianopia. The Wassermann reaction was negative.

Because of the alarming symptoms the patient was transferred to the neurosurgical unit of the Johns Hopkins Hospital. Craniotomy disclosed a subdural hemorrhage. This was removed as completely as possible; the wound was closed, and a decompression was left; the condition of the patient was desperate. He gradually improved; the convulsions ceased, and he was able to talk and even to

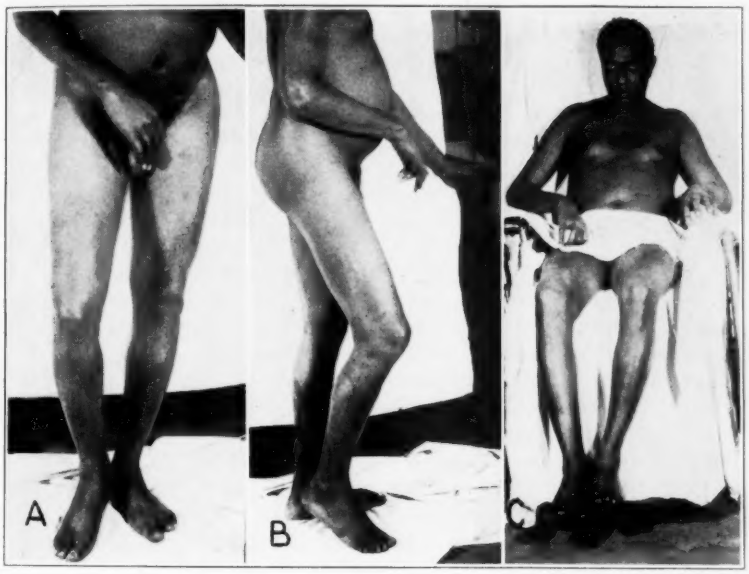

Fig. 2 (case 2).—The position of the leg in certain cases of hemiplegia is shown. This patient had operations for the relief of jacksonian convulsions associated with a subdural hematoma. The leg is externally rotated and flexed at the hip and knee. It was possible to rest the ball of the foot on the floor. The position is well adapted to sitting in a chair.

walk. However, the wound continued to bulge at times, with increase in the symptoms, and injections of air showed greatly distended ventricles. It was necessary to relieve the hydrocephalus several times and even to open the skull and remove further clots. As a result, a fistula became established between the lateral ventricle and the subarachnoid space. The patient was then transferred to the hospital for chronic diseases. The records are exceedingly meager; it has not been possible to learn when the present picture first appeared.

Aphasia and right hemiplegia persisted after the operative treatment. The patient answered "des" to every question and seldom any other word. During the

day he sat in a wheel-chair, played checkers and hummed tunes, although he could no longer sing the words. With the left hand he showed how formerly he played the piano.

Examination revealed the patient to be overnourished and cooperative (fig. 2 *C*). Over the left parietal region was the depressed scar of the former operation. There was right homonymous hemianopia. The facial muscles moved equally well on each side, and the tongue was protruded in the midline. Comprehension was poor; he touched the head with the hand on command but did not understand the request to touch the nose with the left hand.

When the patient stood the right shoulder was lower than the left and the abdomen was more prominent on the right (fig. 2 *A*). The right arm was partially flexed at the elbow, and the fingers were somewhat flexed (figs. 2 *A* and *B*). He was able to raise the arm at the shoulder above the horizontal level so as to place the fingers on top of the head, but there was almost no power of extension of the elbow, wrist or digits. A positive Hoffmann response was obtained on stimulation of any of the fingers; there was not only well sustained wrist clonus but also finger clonus. The abdominal and cremasteric reflexes were absent on the right.

The leg was flexed at the hip and knee, and the foot showed plantar flexion (figs. 2 *A* and *B*). It was possible for the patient in the upright position to rest his weight on the toes of the right foot and to stand. The adductor muscles of the thigh showed considerably increased tone, and the leg was externally rotated. Considerable power of voluntary flexion was present in the leg. A marked reflex was obtained from the hamstring muscles; the knee jerk was active if the leg was further flexed before this reflex was elicited. There was ankle clonus.

Attempts to obtain a Babinski reflex were followed by a general movement of withdrawal with flexion at the hip, knee and ankle but no movement of the toes. The toe component of the reflex was obtained from two portions of the body. Painful stimulation of the right axilla or of the right side of the chest in the midaxillary line caused fanning of the toes of the right foot followed by dorsiflexion of the great toe; at the same time there were flexion of the hemiplegic arm and internal rotation of the leg. Dorsiflexion of the normal foot against resistance also caused fanning of the toes and dorsiflexion of the great toe on the hemiplegic side.

The associative reflexes were not as stereotyped as in case 1. In general the responses were more marked in the hemiplegic arm than in the leg. Flexion of the neck against resistance caused further flexion of the hemiplegic arm, and extension of the neck caused extension of the arm. When the chin was turned toward the side of the lesion the arm extended at the elbow was adducted and was internally rotated, while at the same time the leg was flexed at the knee and hip. Turning the chin toward the opposite side caused flexion and abduction of the arm but no movement of the leg. A firm handgrasp on the normal side produced flexion of the hemiplegic arm and extension of the leg. If the left arm was held extended at the elbow against resistance, the right arm was flexed and externally rotated and the right leg flexed. If the left arm was held flexed at the elbow, the hemiplegic arm was flexed and adducted and the leg internally rotated and extended. Finally, flexion of the left leg at the knee against resistance caused flexion of the right leg. Associated movements, therefore, induced either flexion or extension of the hemiplegic leg, but the flexor movements predominated.

The position of the paralyzed extremities was adapted ideally to a sitting posture in a wheel-chair, as is evident from the photograph (fig. 2 *C*). The arm fixed in a position between flexion and extension rested on the arm of the chair, and the leg adapted itself to a sitting position.

As the patient was able to bear his weight on the toes of the hemiplegic foot, an effort was made to teach him to walk in order to learn the effect of exercise on the posture of the extremity. He cooperated well and practiced walking with a cane for support many hours each day. Walking became worse instead of better, for strong clonus developed in the paralyzed leg when weight was placed on it, which made balance difficult. No change in the amount of flexion of the extremity was noted following this exercise.

The patient overacted emotionally to sensory examinations, and the responses were much more marked on the abnormal side. Thus, pinprick was definitely disagreeable and was tolerated poorly on the hemiplegic side whereas the response on the uninjured side were relatively normal. He stated, however, that pinprick felt sharper on the normal side. Likewise, the reaction to vibratory stimuli was more marked on the paralyzed side of the body. It was impossible to make an adequate sensory examination because of the aphasia. The patient gave the general impression of marked emotional instability.

CASE 3.—F. H., a Negro aged 38, was seen soon after the accident which produced the characteristic deformity. The hemiplegia was on the left, and the patient was able to talk normally. While sitting on the porch "a friend" struck him on the right side of the head in the parietal region with a piece of wood; the force was sufficient to cause a depressed fracture of the skull. He was taken to the hospital at once and regained consciousness in a few hours.

When seen two weeks after the accident the patient suffered such severe pain on the slightest movement that he remained lying in one position on his back constantly. If the left arm or leg was moved or touched, he screamed with pain. There was weakness of the facial muscles on the left, which was particularly marked in the orbicularis oculi so that it was impossible to close the eye tightly. The tongue was protruded to the left. Expansion of the chest was deficient on the left. The left arm was slightly abducted and lay on a pillow. The elbow, wrist and fingers were extended. There was marked edema of the hand and wrist. The left leg was externally rotated and flexed at the hip and knee. The ankle was flexed. There was great edema around the knee and in the ankle and foot. Any attempt to flex the elbow, extend the knee or, indeed, move the left arm and leg gave rise to such severe pain that the deep reflexes were not obtained. Attempts to elicit a plantar reflex gave rise to general withdrawal of the leg and pain. The abdominal and cremasteric reflexes were absent on the left.

Response to pinprick was diminished on the left side, so that the pin could often be thrust almost through the skin without the patient's knowledge. When he perceived it, unusual pain was experienced. The deep structures were hyperesthetic and extremely sensitive to any stimuli.

For two months the patient's condition remained unchanged. The hyperesthesia and edema of the paralyzed extremties persisted. There was generalized wasting of the muscles on the left side of the body. Then gradually the pain decreased and the localized edema subsided, so that at the end of eight months the patient was fairly comfortable. He still complained on any passive movement of the hemiplegic arm or leg. The extremities remained fixed in the position already described.

CASE 4.—N. G., a white man aged 64, with chronic alcoholism and mental deterioration, had two cerebral vascular accidents affecting the left side of the body within six months. The family stated that the left leg became flexed immediately after the second acute seizure and remained in this position. Figure 3*A* shows the extreme flexion of the leg; the arm was extended at the elbow, and the fingers were only partially flexed. Pinprick caused a stronger reaction on the left

side of the body than on the right, although it felt sharper on the normal side. Emotionally the patient was very unstable. There was considerable spontaneous pain on the hemiplegic side, particularly in the leg.

CASE 5.—C. M., a Chinese, had right hemiplegia with aphasia. Figure 3*B* shows the external rotation of the leg and flexion at the hip and knee. The arm was in a typical hemiplegic position. In this case all attempts to demonstrate associated movements led to marked flexion of the hemiplegic leg, which lifted the heel well off the table; the toes were flexed during this response. This patient was unusually emotional. Pinprick was disagreeable on the hemiplegic side.

CASE 6.—C. L., an elderly Negro, who was admitted to the hospital for chronic disease with marked arteriosclerosis and signs of cardiac failure, later had left hemiplegia. He was very short of breath and in considerable distress directly after the cerebral accident. There was conjugate deviation of the eyes to the right, and it was impossible to move them beyond the midline. Left hemianopia was present. The face showed loss of tone and voluntary movement on the left; there was deviation of the tongue to the left. There was complete loss of all tone and power of movement in the left arm. The paralyzed leg was externally rotated and flexed at the knee and hip. When the leg was extended passively it at once became flexed again. The paralyzed extremities were cold, and there was some

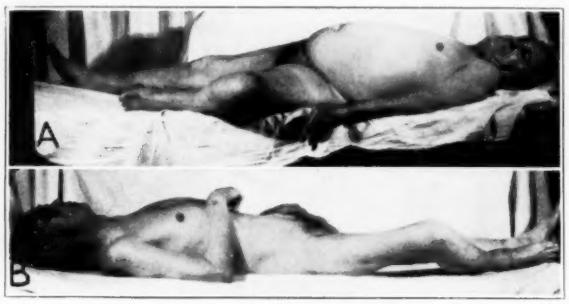

Fig. 3.—Two patients who demonstrated flexion of the leg associated with hemiplegia.

edema of the wrist and ankle. Sensory examination revealed complete loss of pain sense and temperature sense on the hemiplegic side. Vibratory sense and sense of passive movement also were lost on the left. There was a positive Babinski sign on this side.

Six days after the cerebrovascular accident the patient died. Examination of the brain revealed thrombosis of the middle cerebral artery. The softening extended from the surface of the cortex into the internal capsule, putamen, globus pallidus and lateral nucleus of the thalamus.

One other case in which the brain was examined revealed similar widespread softening of the internal capsule, corpus striatum, ansa lenticularis and lateral nucleus of the thalamus.

COMMENT

From the data presented it is possible to comment on the factors responsible for the production of this unusual posture in hemiplegia. Is the change of tonic pattern dependent on the habitual posture of the patient since the cerebral injury? The posture is admirably adapted

to sitting in a chair. However, in two cases flexion of the leg appeared within a few days after the vascular accident. Three of the patients sat in a chair during the day, but two with marked deformity remained in bed throughout the period of the illness. Thus, as the flexion of the leg may appear only a few days after the vascular accident and appears no matter whether the patient sits up or lies in bed continually, it cannot be attributed to the habitual posture.

We are convinced further that the deformity is not due to primary arthropathy. None of the six patients reported on presented other evidences of arthritis, and any changes in the joints are secondary to the deformity from some other cause. In like manner the contracture cannot be considered the cause, for a primary contracture is dependent on initial injury of peripheral structures. Following an initial lesion of the central nervous system it is necessary to consider changes in tone or tonic patterns dependent on the cerebral damage which determine the future position of the extremities and may indeed lead to contracture secondarily. This leaves only one explanation for consideration: The pattern of hypertonus in these cases is dependent on the type of injury in the nervous system. We are led, therefore, to a consideration of the theoretical interpretation of posture in hemiplegia and to theoretical comment on the present cases.

Theoretical Interpretation of the Posture in Hemiplegia.—Sherrington in 1897 described the attitude of common laboratory mammals after transection of the neuraxis at the level of the midbrain and removal of the forebrain. At once an increased tonus appeared in the antigravity muscles. When other animals were studied in this way it was found that in each species the tone appeared in the antigravity muscles, even though these were not necessarily the extensor muscles of the body. For example, Richter and Bartemeier [7] (1926) found that the hypertonus in the decerebrate sloth occurred in the flexor muscles of all four extremities. The sloth normally hangs from the limbs of trees, and the flexors are the antigravity muscles.

This provides an explanation for the fact that hypertonus in the cat is present in the extensor muscles of all four extremities, whereas in man the spasticity is maximal in the flexor muscles of the arm and the extensor muscles of the legs. The pattern of tone in the muscles of man has been adapted to the erect posture. When the arms are freed from their function as locomotor props and hang freely at the side, the flexor muscles of the arms instead of the extensors resist gravity. In patients with hemiplegia there is accentuation of the normal antigravity pattern of tonus of the human family. Severance of the

7. Richter, C. P., and Bartemeier, L. H.: Decerebrate Rigidity in the Sloth, Brain **49**:207, 1926.

corticospinal tract on one side in man, however, is not anatomically equivalent to decerebration or even hemidecerebration of animals. The functional value of different pathways in the nervous system controlling tonus varies greatly in different species, and there is always a tendency for the dominant components to shift in the cephalic direction in the neuraxis (Langworthy,[8] 1932).

Theoretical Interpretation of Cases of Hemiplegia with the Leg in Flexion.—From consideration of the cases described in this paper it has been concluded that the variation in posture is dependent on the position and extent of the lesion in the nervous system. The injury is not confined to the pyramidal tracts, but involves other pathways, producing a variation of the usual picture. The tonic pattern in decerebrate animals is not constant; preparations of cat are from time to time observed to show flexor instead of extensor rigidity. Flexor rigidity has been discussed in particular by Bazett and Penfield[9] (1922). This phenomenon is undoubtedly dependent on a variation in the extent of the lesion, but the pathways controlling tone are so complicated that a satisfactory anatomic explanation has not been given.

Many observers hold that increased flexor tone of the legs in man is present only after severe lesions of the spinal cord, so that encephalic motor control is lost and the cord is completely transected. This type of injury was well described by Riddoch[10] in 1917 in soldiers with transection of the spinal cord. The most remarkable feature during the period of maximal reflex activity in these patients is the mass reflex. Stimulation of the sole of one foot caused contraction of all the muscles innervated from below the level of the lesion, emptying of the bladder and marked sweating. The legs took up a position of flexion, and the condition was known as paraplegia in flexion.

If the pyramidal tracts alone are injured in the cord the legs are held in extension owing to the hypertonus that develops in the extensor muscles, and the condition is called paraplegia in extension. The pyramidal tracts are particularly sensitive to pressure, and paraplegia in extension may be the clinical picture when an extramedullary tumor presses on the cord. Later, if the pressure becomes greater so that a physiologic transection of the cord is produced, the legs become flexed and the typical appearance of paraplegia in flexion intervenes.

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8. Langworthy, O. R.: The Control of Tonus After Injuries of the Brain or Spinal Cord of Man, Medicine **11**:225, 1932.

9. Bazett, H. C., and Penfield, W. G.: A Study of the Sherrington Decerebrate Animal in the Chronic as Well as in the Acute Condition, Brain **45**:185, 1922.

10. Riddoch, G.: The Reflex Functions of the Completely Divided Spinal Cord in Man, Compared with Those Associated with Less Severe Lesions, Brain **40**: 264, 1917.

If one assumes that the change from paraplegia in extension to paraplegia in flexion is due to loss of future motor influence from the brain acting on the cord, there is no reason why these influences should not be blocked above the level of the spinal cord. In the cases of hemiplegia with the leg in flexion we believe that this was the cause and that the motor control was injured in the brain. The tonic reflexes in the neck were active in the cases reported here, and no abnormalities of cerebellar or vestibular control were demonstrated. The damage did not involve pathways extending from the brain stem to the cord but rather pathways from the forebrain.

It is unfortunate that we have been unable to carry out more extensive pathologic studies, but it is doubtful whether exact information would be obtained by this means. The lesion produced by hemorrhage or thrombosis in the forebrain is so widespread that it would be difficult to determine the portion of the destroyed area responsible for the abnormality. The pathologic reports in the French cases included mention of diffuse lesions involving the cortex, thalamus and basal ganglia. The pyramidal tracts run a long course in the brain, and variable pictures of hemiplegia should be produced depending on the level of damage and the contiguous structures involved. This has been taken into account in the case of the brain stem, where palsy of the cranial nerves makes a precise localization possible, but there has been less effort at exact localization in the forebrain.

We are able now to offer two possible explanations for the flexion of the leg and tendency to extension of the arm in hemiplegic patients. The emotional instability, hyperesthesia and occasional spontaneous pain suggest involvement of the lateral nucleus of the thalamus. In the one patient seen soon after injury the pain and hyperesthesia were severe but showed a tendency to diminish with time. No tremor or ataxia of the extremities was ever noted. It might perhaps be possible to accept Walshe's explanation that the flexion of the leg is due primarily to the pain. It is not clear, however, why a painful arm would be more comfortable when extended at the elbow or a leg when flexed at the hip and knee.

It is difficult to believe that the posture is dependent on pain following a lesion of the thalamus. Rather, the sensory change demonstrates that the injury involved structures deep in the forebrain. There is other evidence that the damage was widespread; several of the patients showed aphasia and hemianopia.

The other theory suggests a combined lesion of the pyramidal tract and efferent pathways from the corpus striatum. When there is hypertonus of all the muscles of the body in a case of parkinsonism due to lesions of the motor nuclei closely connected with the corpus striatum,

there is a tendency for the trunk and extremities to assume a position of flexion. The legs often become fixed in flexion in the terminal stages of the disease after the stiffness is so great that the patient is no longer ambulant. The tendency for the legs to become fixed in flexion appears to be greater if the pyramidal tracts are involved in the damage.

Noica[11] (1909) noticed that children born with defects of the pyramidal tract and corpus striatum often hold the legs fixed in flexion so that they are never able to learn to walk. Operations to straighten the legs did not influence the condition, as the extremities returned at once to their former position.

There are certain types of cerebral lesions which appear to produce increased flexor tone of the extremities. Patients with so-called Little's disease with or without athetosis may present flexion of the legs which makes walking impossible. Patients with widespread lesions of both hemispheres often have the legs fixed in flexion. Parkinson's disease and severe but compensated hydrocephalus may be associated with flexor contracture.

We submit these cases of hemiplegia with the leg in flexion and express the belief that the lesion was confined to the forebrain. The peculiar posture may be dependent on pain due to injury of the thalamus or to injury of both the pyramidal tract and the afferent pathways from the corpus striatum or may have some other explanation not yet suggested.

SUMMARY

Patients with injury of the pyramidal tract producing hemiplegia show abnormalities of tone that usually conform to a stereotyped pattern: The arm is held in a flexed position and the leg in extension. Cases are reported here in which the leg was externally rotated and flexed at the hip and knee so that standing and walking were impossible. The position of the arm was variable; it was often extended at the elbow. The patients were emotionally unstable, and hyperesthesia of the affected side could be demonstrated. Some complained of severe pain in the affected arm and leg. After lesions of the central nervous system any contracture that is present must be secondary, in the position imposed by the abnormality of tone. The flexor position of the leg in two cases was observed within a few days after the vascular accident. In these patients it is believed that the neural lesion was confined to the forebrain. The lesions were extensive and in several cases produced aphasia and injury of the lateral nucleus of the thalamus. Two theories have been advanced in an attempt to explain these findings.

11. Noica, M.: Sur la contracture des membres inférieurs en flexion, Rev. neurol. **17**:228, 1909.

THE CEREBRAL CIRCULATION

XLI. VASCULAR RESPONSES TO (A) HYPERTONIC SOLUTIONS AND (B) WITHDRAWAL OF CEREBROSPINAL FLUID

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A. HYPERTONIC SOLUTIONS

The purpose of this paper is to describe some of the vascular changes in the brain following the administration of strongly hypertonic solutions and to compare these changes with those following simple withdrawal of cerebrospinal fluid.

In a previous paper of this series [1] it was reported that blood vessels in the pia constricted after intravenous or intraperitoneal injections of hypertonic solutions. This report was based on few experiments and was of a preliminary character. Recently, with improved technic the earlier work has been repeated and a much larger series of experiments performed. We believe now that the previous conclusions should be modified.

Method.—Cats anesthetized with amytal (sodium barbiturate) or dial [1a] (diallyl barbituric acid and ethyl carbamate) given by intraperitoneal injection were used in these experiments. Observation and measurement of pial vessels were carried out through a cranial window,[2] and photomicrographs were taken with a Leica camera, both in black and white and in color on Lumière film. Small windows (12 or 16 mm. in diameter) were used, for it was found that the original 19 mm. windows often caused pressure against the surface of the brain.[3] This pressure sometimes flattened veins and even arteries traversing the more prominent convolutions and gave a false appearance of increase in caliber. Subsequently, when dehydration caused shrinkage in the volume of the brain, the pressure against the

This research was aided by a grant from the Josiah Macy Jr. Foundation.

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1. Wolff, H. G., and Forbes, H. S.: Cerebral Circulation: IV. The Action of Hypertonic Solutions: Part I., Arch. Neurol. & Psychiat. **20**:73 (July) 1928.

1a. The dial was furnished by the Ciba Company, New York.

2. Forbes, H. S.: Cerebral Circulation: I. Observation and Measurement of Pial Vessels, Arch. Neurol. & Psychiat. **19**:751 (May) 1928.

3. Windows with curved instead of flat glass were tried, the radius of curvature being approximately that of the skull. These were fairly satisfactory but were open to one serious objection: If the brain was pushed upward the flow through some of the pial vessels might be interfered with by pressure against the edges of the trephine hole. Since the point of interference lay outside the visible field, it was difficult to recognize an error arising from this source. Consequently experiments in which the curved glass was used were discarded.

glass was released and the horizontal diameters of the vessels became less, giving a false appearance of constriction. Also local blanching was followed by redness of the surface of the brain when the pressure was reduced. At other times, owing to operative trauma, the pial arteries were dilated before any experimental procedure was undertaken. Under such abnormal circumstances the arteries usually became narrower after the injection of a hypertonic solution. The results in some of the experiments reported in the previous paper [1] can be explained on this basis. With the smaller windows and with extreme care to avoid trauma it was usually possible to prevent accidental vasodilatation at the start of an experiment.

The initial cerebrospinal fluid pressures were usually lower than those recorded by Weed and McKibben.[4] This was due partly to the effect of different anesthetics. Weed used ether, which causes a pressure about 30 mm. higher than does amytal or dial. Also we withdrew 1 or 2 cc. of fluid from the cistern before inserting the window. This was done in order to lower the surface of the brain and prevent contact with the glass of the window. The wide variation in the level of the cerebrospinal fluid pressure at the beginning of the experiment depended somewhat on the varying amounts of fluid injected beneath the window to replace the fluid removed from the cistern.

As hypertonic solutions a 30 per cent solution of sodium chloride and a 50 per cent solution of urea in water were used. These were injected by means of a syringe into the vein of the leg or into the peritoneal cavity. The dose was the smallest which was found to cause a maximum fall in cerebrospinal fluid pressure. In order to compare the effect of urea with that of sodium chloride the attempt was made to use amounts of the two solutions which would produce approximately the same osmotic effect. This dosage was not always strictly adhered to, however (tables 1 and 2). For the intraperitoneal injections the average dose of urea was somewhat larger than the molar equivalent dose of sodium chloride. With the intravenous injections the dosages of both sodium chloride and urea, though approximately isosmotic one with the other, were reduced below those used in the intraperitoneal injections, in order to avoid a serious fall in blood pressure. The results of thirteen experiments were discarded: eight in which there was hemorrhage beneath the window and five in which the brain was strongly pressing against the glass or in which the artery was dilated by accidental manipulation at the start of the experiment.

Observations and Comment.—Twenty-eight experiments were performed on twenty-eight cats. Intraperitoneal injections elicited the following results:

In figures 1 and 2 is shown the prevailing type of response as well as the individual variations. The pial arteries began to dilate within from five to ten minutes of the injection and reached their maximum size from twenty to thirty minutes later. Soon after this they began to return slowly to their original diameters; sometimes they constricted to less; sometimes they remained partially dilated. Often the dilatation was preceded by brief fluctuations in the size of the arteries and a transient rise of a few millimeters in cerebrospinal fluid pressure before

4. Weed, L. H., and McKibben, P. S.: Pressure Changes in the Cerebrospinal Fluid Following Intravenous Injection of Solutions of Various Concentrations, Am. J. Physiol. **48**:512 (May) 1919.

it began its steady fall. The veins and venules showed little change in size at first; later they dilated. The veins and the surface of the brain became at first redder and later more cyanotic and darker as the veins dilated. The venous flow became noticeably slower during this period.

TABLE 1.—*Results of the Intraperitoneal Injection of Hypertonic Solutions on the Cerebrospinal Fluid Pressure*

Experiment	Dose, Cc. per Kg.	Cerebrospinal Fluid Pressure, Mm. Ringer's Solution		Rate of Fall of Cerebrospinal Fluid Pressure, Mm. per Min.
		Before Injection	Low Point	
		A. Urea		
1	8	32	—175	4.0
2	9	17	—277	7.4
3	10	9	—287	7.4
4	10	65	—157	4.2
5	8	45	—168	2.5
6	10	42	—213	4.8
7	10	75	—163	5.3
8	10	60	—186	5.0
9	8	60	—300+	
10	8	120	—130	4.4
11	8	72	—240	6.8
		B. Sodium Chloride		
12	5.0	49	—196	4.2
13	5.0	53	—161	3.6
14	6.5	52	—183	4.1
15	5.0	57	—196	4.8
16	5.0	81	— 68	2.8

TABLE 2.—*Results of the Intravenous Injection of Hypertonic Solutions on the Cerebrospinal Fluid Pressure*

Experiment	Dose, Cc. per Kg.	Rate of Injection, Cc. per Min.	Cerebrospinal Fluid Pressure, Mm. Ringer's Solution		Rate of Fall of Cerebrospinal Fluid Pressure, Mm. per Min.
			Before Injection	Low Point	
			A. Urea		
17	5.0	2.5	39	—25	3.2
18	7.0	2.1	74	—30	2.1
19	5.0	0.7	58	—84	2.7
20	3.0	0.6	70	—31	7.8
21	3.5	0.9	61	—13	2.1
22	5.0	1.0	55	—80	4.2
23	4.0	1.0	50	—28	4.2
			B. Sodium Chloride		
24	3.0	0.7	37	—16	1.4
25	3.5	0.6	24	—42	2.9
26	3.5	1.0	93	— 5	2.4
27	3.5	1.5	70	—66	5.2
28	3.5	0.3	67	— 6	1.4

Intravenous injections were followed by less uniformity of response than intraperitoneal injections (figs. 4 and 5). An abrupt fall in blood pressure often occurred during injection into a vein. (This was especially true with sodium chloride.) In order to prevent circulatory failure, therefore, it frequently was necessary to lessen the speed of injection at once or even to stop the injection for a moment. These irregularities in the rate of injection gave rise to many of the individual variations in response shown in figures 4 and 5. The dilatation of pial

arteries, which was the most conspicuous reaction in the experiments with sodium chloride, began during the injection and reached its height at the end of this period. During the next half-hour usually the arteries regained their former size and then constricted still further, remaining thus for more than an hour. With urea, if injected slowly, the arteries either showed little change or constricted without previous dilatation.

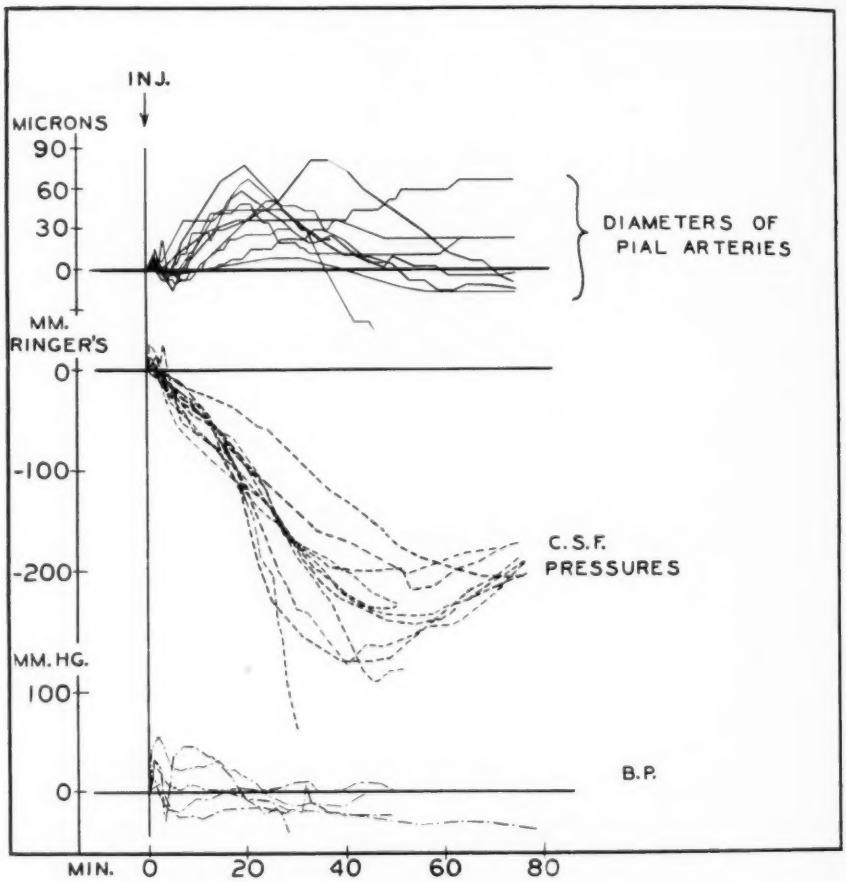

Fig. 1.—Effect of intraperitoneal injection of a 50 per cent solution of urea. Individual charts for experiments 1 to 11 are included in this group. In figures 1 and 2 *INJ.* indicates the time at which the injections were made.

In constructing the charts shown in figures 1, 2, 4 and 5 the individual charts of the several experiments were superimposed one on the other. The diameters of the pial arteries and the cerebrospinal fluid and blood pressures during the control periods of observation were reduced to a common base-line. The ordinates represent changes in diameter of the pial arteries expressed in microns, changes in cerebrospinal fluid pressure in millimeters of Ringer's solution and changes in femoral arterial pressure in millimeters of mercury. The abscissas represent the time after the injection, expressed in minutes.

During a rapid injection of urea (and still more was this true of sodium chloride) a sudden drop in blood pressure was found to occur immediately before or synchronously with the arterial dilatation. The arterial response to a very rapid injection of sodium chloride was similar to that after a similar injection of urea (fig. 6). Intravenous injection of either sodium chloride or urea caused a total decrease in cerebrospinal fluid pressure only one-third as great as that after intraperitoneal injection [5]; also the cyanosis of the veins was less marked. The dilatation

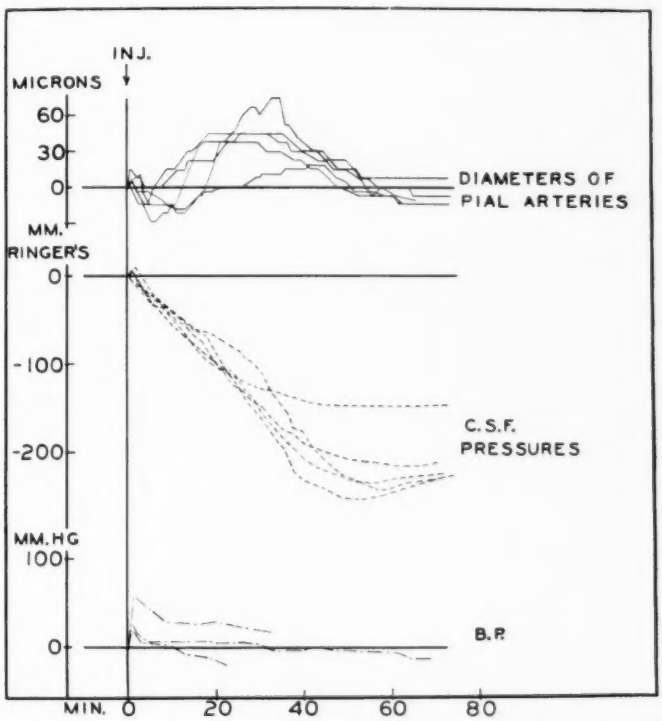

Fig. 2.—Effect of intraperitoneal injection of a 30 per cent solution of sodium chloride. Individual charts for experiments 12 to 16 are included in this group.

5. This difference can be explained as follows: After intravenous injection of a hypertonic solution the blood volume shows a prompt increase; the venous pressure is raised, and the fall in cerebrospinal fluid pressure is delayed. Also equilibrium between the intravascular and extravascular osmotic pressures is probably reached sooner than after intraperitoneal injection. After the latter procedure the blood volume is decreased by the passage of fluid into the peritoneal cavity, as well as by elimination through the kidneys. Though we made no actual determinations of the blood volume, hematocrit readings show changes too large to be accounted for except by alterations in the total volume of the plasma. These changes are consistent with an increase in blood volume after intravenous injection and a decrease after intraperitoneal injection of a hypertonic solution.

of the veins after intravenous injection either was less than after intraperitoneal injection or was entirely absent.

In addition to the changes outlined, the reaction of the vessels was affected to an unknown extent, in spite of precautions, by the presence or absence of slight trauma, by occasional contact between the surface of the brain and the window and by the removal of differing amounts of cerebrospinal fluid from the cistern prior to insertion of the window. These technical differences account probably for some of the variations in response to similar amounts of the same solution injected in a similar manner. Still other variations may have been due to differences in the physical condition of the animals and to differences in age, fluid balance, depth of anesthesia, etc. Changes in any of these factors might affect the rate of absorption of the hypertonic solutions and hence the rate and extent of response. Gross changes in respiration were controlled by using artificial respiration throughout some of the experiments.

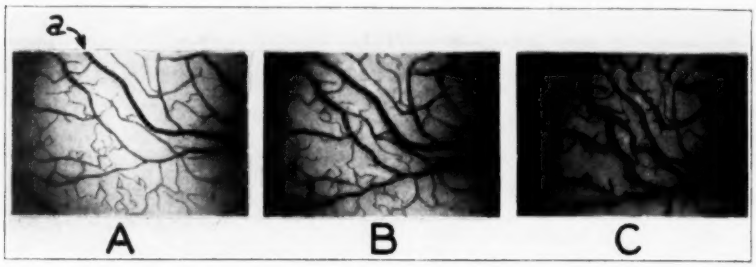

Fig. 3 (experiment 9).—Changes in the appearance of pial vessels after the intraperitoneal injection of a 50 per cent solution of urea. *A*. Before the injection; cerebrospinal fluid pressure + 60. *B*. Eighteen minutes after the injection; cerebrospinal fluid pressure —60. *C*. Thirty-nine minutes after the injection; cerebrospinal fluid pressure —300. The pial artery is indicated by *a*; the other vessels in the field are veins. In *B* the artery is dilated, and the veins have begun to dilate. In *C* the artery has constricted again; the veins are dilated, and the whole field is much darker. This condition is referred to in the text as the "delayed reaction." The photomicrographs in this figure and in figures 7, 8 and 10 were taken with a Leica camera and Persenso film, using a low power lens, objective 3, ocular 10. They were exposed and printed under uniform conditions of light and time; therefore, any change in the darkness of the background represents an actual increase in the redness and darkness of the surface of the brain. It will be seen that the degree of darkness in these photographs varies directly with the degree of dilatation of the venules.

In order to test the effect of the injected solution, aside from changes in intracranial pressure, we carried out the following additional experiments:

A concentrated solution of sodium chloride or of urea was applied locally to the surface of the brain by injecting the solution beneath

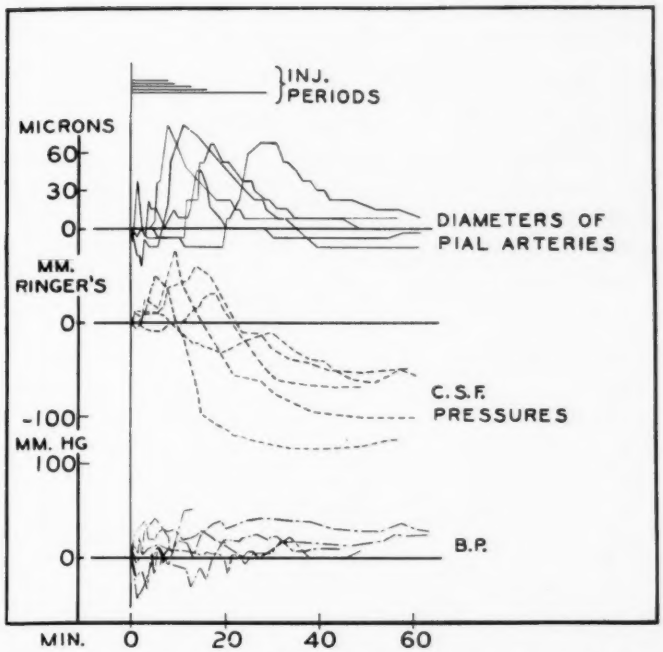

Fig. 4.—Effect of intravenous injection of a 30 per cent solution of sodium chloride. Individual charts for experiments 24 to 28 are included in this group. In the charts in figures 4 and 5 each horizontal line in the group labeled *INJ. PERIODS* represents the length of time taken for the injection in a single experiment.

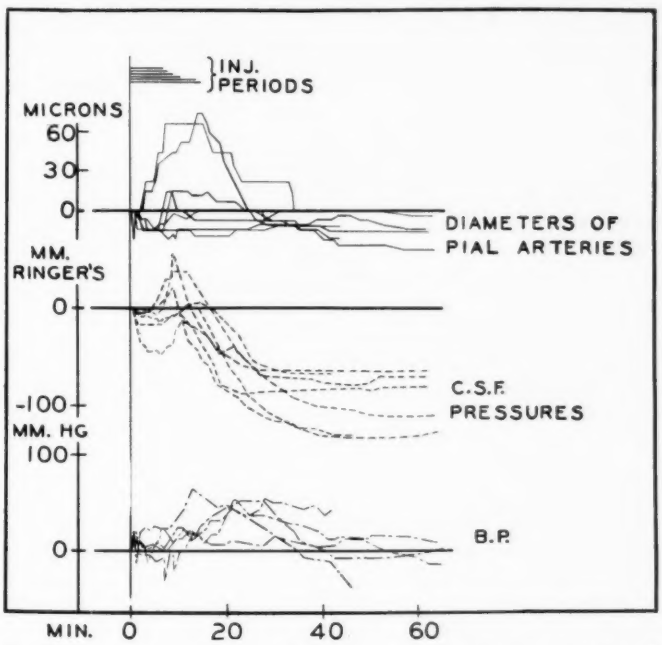

Fig. 5.—Effect of intravenous injection of a 50 per cent solution of urea. Individual charts for experiments 17 to 23 are included in this group.

the cranial window and allowing an equal volume of cerebrospinal fluid to escape. No change in intracranial or in blood pressure resulted, yet the pial arteries dilated to an extreme degree. Ringer's solution injected in similar manner caused no change in the caliber of the vessels. Another experiment was even more significant. Urea (50 per cent solution) was injected into the peritoneal cavity, and the usual fall in cerebrospinal fluid pressure was prevented by the gradual addition of warm Ringer solution beneath the window. Under these conditions, just as when

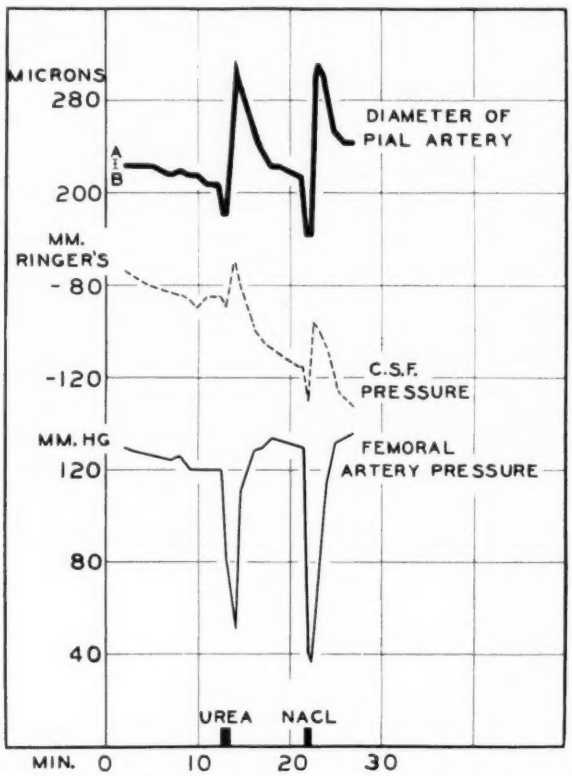

Fig. 6.—Effect of hypertonic solutions of urea and sodium chloride when injected rapidly into a vein.

In this figure and in figure 9 ordinates represent the actual diameter of the pial artery, expressed in microns, the cerebrospinal fluid pressure in millimeters of Ringer's solution and the femoral arterial pressure in millimeters of mercury; the abscissas show time expressed in minutes. The broad line, which indicates the diameter of the pial artery, is so plotted that its upper edge records the correct measurements and time relations. The short line *A–B* is the extent of the change in the diameter which could be measured accurately. A change of one-half this extent is of doubtful validity.

the pressure was allowed to fall, the pial arteries dilated. In one of these experiments in which the pressure had been kept from falling

for fifty-eight minutes, the pressure was suddenly decreased from 30 to —190 mm. by withdrawing fluid from the cistern. The arteries at once constricted. In this experiment the behavior of the veins too was of particular interest. After the injection of urea they were somewhat dilated, but when the cerebrospinal fluid pressure was suddenly lowered, instead of constricting like the arteries, the veins and venules dilated still further (fig. 8).

The findings in the experiments thus far seem to warrant the following conclusions:

The prompt dilatation of the pial arteries after the injection of a hypertonic solution of urea or sodium chloride is due not to the fall in cerebrospinal fluid pressure but to a more immediate action. This action is exerted probably on the walls of the arteries themselves, as evidenced by their response to local application of the solution. The increased redness of the veins at this time is due to the increased rate of blood flow through the dilated arterioles.

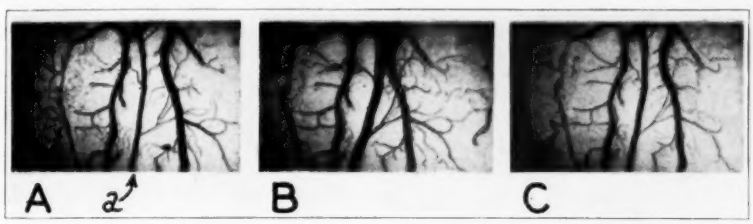

Fig. 7 (experiment 25).—Changes in the appearance of pial vessels after the intravenous injection of a 30 per cent solution of sodium chloride. *A*. Before the injection; cerebrospinal fluid pressure + 25. *B*. Two minutes after the injection; cerebrospinal fluid pressure + 49. *C*. Twenty-eight minutes after the injection; cerebrospinal fluid pressure —42. In *B* the "immediate reaction" is shown. The pial artery (*a*) is extremely dilated. In *C* it has nearly returned to its original diameter. There is no dilatation of the veins or increase in darkness, as shown in figure 3.

The subsequent dilatation of the venules, developing during the fall in cerebrospinal fluid pressure, can be explained on the basis of the following sequence: shift of water from the subarachnoid and tissue spaces into the blood stream, lowered extravascular pressure with lessened external support for the extremely thin-walled pial venules (or actual outward traction on these structures) and consequent dilatation of the latter vessels. Here there is local but direct evidence that an increased volume of blood in the venules within the skull compensates for the diminished volume of cerebrospinal fluid. These observations support the statement of Weed, Flexner and Clark,[6] who stressed the

6. Weed, L. H.; Flexner, L. B., and Clark, J. H.: The Effect of Dislocation of Cerebrospinal Fluid upon Its Pressure, Am. J. Physiol. **100**:246 (April) 1932.

importance of the part played by the intracranial venous system rather than the arterial system in this adjustment.

The increase in darkness of the surface of the brain (as evident in black and white photographs) was found (by careful study of color photographs) to be due to an increase both in redness and in cyanosis, giving a deeper purple-red color. This color results chiefly, we believe, from dilatation and cyanosis of the venules in the pia.[7] Possibly, as suggested by Kubie and Hetler,[8] the superficial capillaries in the cortex itself may contribute to the change in color, but this seems improbable, owing to the following observation: When india ink was injected into the carotid artery of a cat (the brain of which was dehydrated by previous intraperitoneal injection of urea) the surface of the brain on gross inspection was dark gray. Microscopic examination, however, showed that the areas between the pial venules were white; no dusky "ground-color" was visible from the injected capillary networks in the cortex.[9] Nevertheless, though we have no evidence as to the behavior

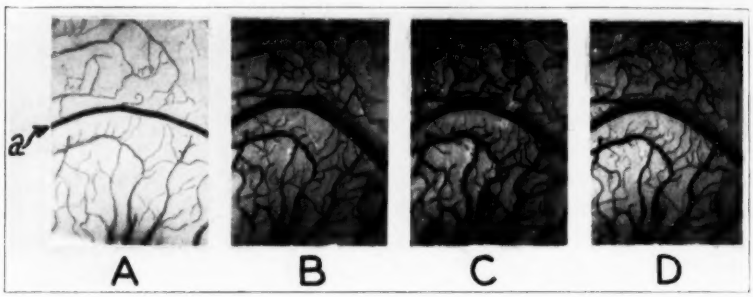

Fig. 8.—Changes in the appearance of pial vessels after the intraperitoneal injection of a 50 per cent solution of urea. The cerebrospinal fluid pressure was artificially maintained at a constant level. *A*. Before the injection; cerebrospinal fluid pressure + 78. *B*. Forty-six minutes after the injection; cerebrospinal fluid pressure + 72. *C*. Six minutes after the cistern reservoir was suddenly lowered; cerebrospinal fluid pressure — 190. *D*. Three minutes after the cistern reservoir was raised again; cerebrospinal fluid pressure + 72. Between *B* and *C* the inflow of warm Ringer solution beneath the window had been stopped, and the cerebrospinal fluid pressure had fallen from + 72 to + 30, showing that the dehydrating effect of the urea was still active.

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7. The action of the arterioles of the pia in causing a change in the color of the surface of the brain is probably slight, since the combined area of the venules is much greater (perhaps twenty times) than that of the arterioles.

8. Kubie, L. S., and Hetler, D. M.: Cerebral Circulation: IV. The Action of Hypertonic Solutions: Part II. A Study of the Circulation in the Cortex by Means of Color Photography, Arch. Neurol. & Psychiat. **20**:749 (Oct.) 1928.

9. This does not imply that the cortical capillaries were not dilated but indicates merely that they were situated too deep to affect the color at the surface.

of the cortical capillaries, we agree with Kubie's general conclusion that in all probability the volume of intracranial blood increases to compensate for the decreased volume of cerebrospinal fluid. Such a readjustment, as Kubie pointed out, is to be expected since, within the limits of elasticity defined by Weed, the Monro-Kellie thesis seems to hold.

The cyanosis of the pial venules deepened as the intracranial pressure fell. Undoubtedly it resulted from the slower blood flow which was clearly visible in these vessels. That the slower flow was not merely local but occurred throughout the brain is indicated by the work of Hamm and Pilcher.[10] These authors found a greater arteriovenous oxygen difference in the brain than in the general circulation of dogs after intravenous injections of hypertonic solutions. They expressed the belief that this indicated a greater slowing of blood flow through the brain than elsewhere.

Explanation for the slower flow through the cerebral venules may be found not only in the venous dilatation but in the lessened gradient

TABLE 3.—*Effects of the Mechanical Lowering of Cerebrospinal Fluid Pressure*

Experiment	Cerebrospinal Fluid Pressure, Mm. Ringer's Solution		Rate of Fall of Cerebrospinal Fluid Pressure, Mm. per Min.	Cc. of Fluid Removed from Cistern
	Before Removal of Fluid	Low Point		
1	43	—245	10.3	3.00
2	43	—260	15.2	2.50
3	40	—228	11.7	4.00
4	42	—275	11.3	2.25
5	41	—287	7.6	3.50
6	58	—280	6.8	3.50
7	58	—270	6.6	3.75
8	38	—258	6.7	3.50

between intracranial and extracranial venous pressures. Evidence for such a change in pressure gradient may be found in experiments on dogs by Weed and Hughson.[11] After intravenous injection of a hypertonic solution of sodium chloride (and subsidence of the immediate reaction) they recorded a decided fall of pressure in the sagittal sinus but a fairly constant pressure in the brachial vein.

B. WITHDRAWAL OF FLUID FROM THE CISTERN

The need of distinguishing more clearly between the chemical effect of the injected solutions on the intracranial vessels and the physical

10. Hamm, L., and Pilcher, C.: Cerebral Blood Flow: I and II. The Effect of Intravenous Administration of Hypertonic and Hypotonic Solutions on the Volume Flow of Blood Through the Brain and on the Cardiac Output and Blood Pressure, Arch. Neurol. & Psychiat. **24**:899 (Nov.) 1930.

11. Weed, L. H., and Hughson, W.: Intracranial Venous Pressure and Cerebrospinal Fluid Pressure as Affected by the Intravenous Injection of Solutions of Various Concentrations, Am. J. Physiol. **58**:101 (Nov.) 1921.

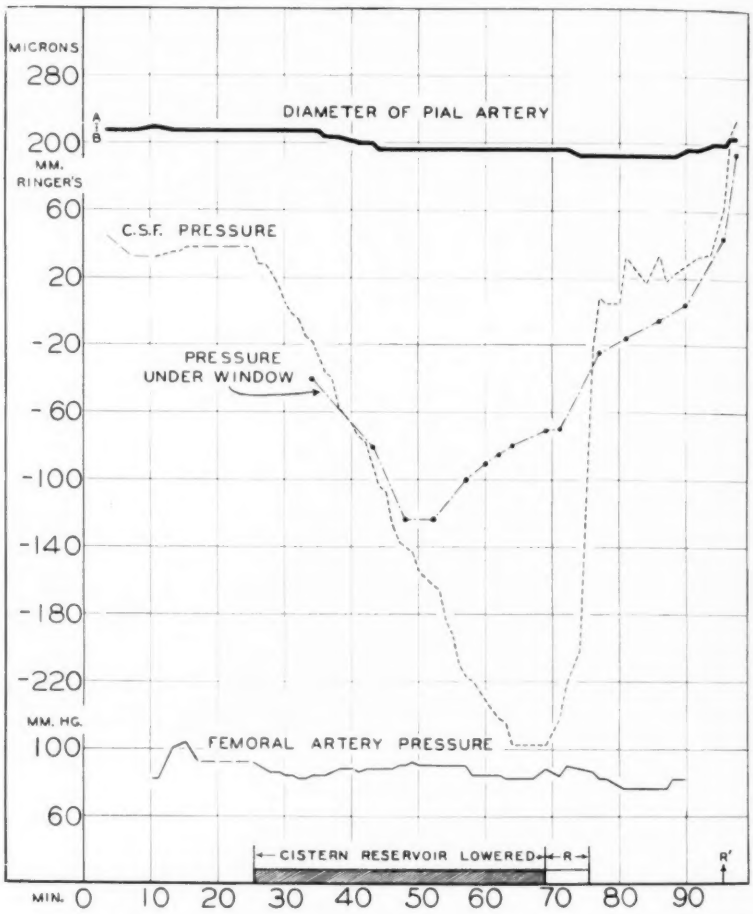

Fig. 9 (experiment 36).—Effect of mechanically lowering the cerebrospinal fluid pressure. A reservoir connected to the cistern manometer was lowered during the period indicated at the bottom of the chart, and 3.5 cc. of cerebrospinal fluid was removed during this period. *R* indicates the period during which the reservoir was raised from a point 258 mm. below the cistern to a level 50 mm. above. Six minutes later only 1 cc. of cerebrospinal fluid had returned to the cistern. Eighteen minutes later 2.5 cc. of the fluid had returned. At *R* the cistern reservoir was raised quickly to a point 250 mm. above the cistern. During the next two minutes the remaining 1 cc. of fluid returned to the cistern. *C. S. F. PRESSURE* indicates the pressure recorded in the cistern manometer; *PRESSURE UNDER WINDOW* refers to the pressure in the space between the window and the arachnoid. It is measured in millimeters of Ringer's solution by the height of the reservoir connected with the bubble manometer and the upper stem of the window. Readings of this height were taken at the points indicated by the black dots.

effect on these vessels resulting from the abrupt fall in cerebrospinal fluid pressure led to the following experiments:

Eight experiments were performed on eight cats. In these experiments the fall of cerebrospinal fluid pressure was brought about by lowering a reservoir which was connected to the manometer tube in the cistern by a 24 gage needle. The reservoir was usually lowered at a uniform rate. By this means from 2 to 4 cc. of cerebrospinal fluid was removed from the cistern in from twenty to fifty minutes.

A bubble manometer was attached to the cranial window so that its lumen communicated with the subdural space. The pressure beneath the window was recorded by this means.

It was found that the pressure fell more slowly under the window than in the cistern, and that by the time the pressure in the cistern had reached a low level (from —250 to —300 mm.) the pressure beneath the window was several centimeters higher than this. In some instances the pressure beneath the window began to rise while the fluid was still being withdrawn from the cistern, giving evidence not only of lack of

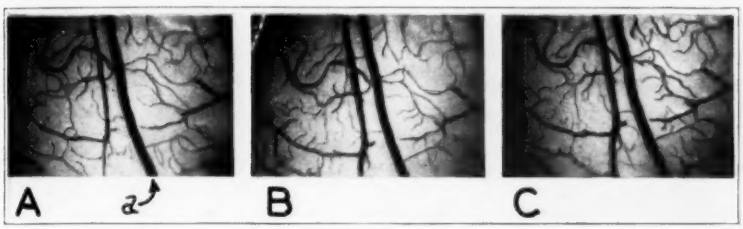

Fig. 10 (experiment 35).—Changes in the appearance of pial vessels after the mechanical lowering of the cerebrospinal fluid pressure. *A*. Control; cerebrospinal fluid pressure + 60. *B*. Twenty-three minutes after starting to lower the cistern reservoir. Two cubic centimeters of cerebrospinal fluid had been withdrawn from the cistern at this time. The cerebrospinal fluid pressure was —20. *C*. Twenty-seven minutes later 3.5 cc. of cerebrospinal fluid had been withdrawn from the cistern. The cerebrospinal fluid pressure was —270; the pressure under the window was —55. The pial artery (*a*) constricted slightly when the cerebrospinal fluid pressure fell but returned to its former size as the pressure fell still further. The veins dilated progressively as the intracranial pressure fell.

free communication between the two localities but of an increase in the bulk of the brain [12] (fig. 9). It was noticed too that the surface of the brain approached the window after several cubic centimeters of fluid had been withdrawn. Furthermore, we found that the total amount

12. The bony tentorium of the cat may, under unusual conditions, such at the rapid withdrawal of fluid from, or its addition to, the cistern, cause obstruction to the passage of fluid through the aqueduct by partial herniation of the brain from above or below. This would permit a difference in pressure above and below the tentorium.

of fluid removed from the cistern could not be reinjected without raising the cerebrospinal fluid pressure far above its initial level. This confirms the result obtained by Masserman [13] on human beings. He found that the rapid removal of 35 cc. or more of fluid by lumbar puncture "diminished the size of the ventriculo-subarachnoid spaces" and that this effect lasted at least eight hours. He concluded that this was due probably to persistent congestion and edema of the central nervous system.

When the intracranial pressure was lowered by withdrawal of fluid the pial arteries usually constricted, but only to a slight extent (fig. 9). When the pressure reached a low level the veins and venules became dilated and cyanotic and the flow distinctly slower. With a low magnification the surface of the brain appeared somewhat darker and more cyanotic as the pressure fell, but this change was much less noticeable than after intraperitoneal injections of the hypertonic solutions.

SUMMARY AND CONCLUSION

A. Hypertonic solutions of sodium chloride and of urea cause two distinct types of reaction on the part of the pial vessels—the first immediate, the second delayed.

The immediate reaction consists of dilatation of the arteries and arterioles and change in color of the venules. These become a brighter red, owing to the increased rate of blood flow. This reaction varies in extent and in duration with changes either in the rate or in the site of injection of the hypertonic solution. Sodium chloride causes a somewhat stronger immediate reaction than does urea.

The immediate reaction is not related to the fall in intracranial pressure. The solutions appear to act directly on the arterial walls.

The delayed reaction consists of dilatation and cyanosis of the veins and venules and a much slower flow through these vessels. The surface of the brain becomes darker red and increasingly cyanotic. These changes are much more evident when the intracranial pressure falls to a low level (from — 100 to — 300 mm.), especially after intraperitoneal injection of a hypertonic solution. The arteries return to their original diameters, or constrict still further, during this period.

B. Reduction of intracranial pressure by removal of cerebrospinal fluid from the cistern causes dilatation of the pial venules, accompanied by cyanosis and a slower flow. These changes, however, are less marked than those seen during the delayed reaction after intraperitoneal injec-

13. Masserman, J. H.: Cerebrospinal Hydrodynamics: IV. Clinical Experimental Studies, Arch. Neurol. & Psychiat. **32**:523 (Sept.) 1934.

tions of hypertonic solutions. Removal of fluid from the cistern causes no dilatation of the arteries but tends rather to constrict them.

It seems safe to conclude that the delayed vascular response of the pia mater to hypertonic solutions is definitely related to the dehydration of tissues and to the great fall in intracranial pressure. The increased volume of blood in the veins and venules within the skull under these conditions is entirely consistent with the revised Monro-Kellie hypothesis. The pial arteries appear to take no part in this adjustment.

CHORDOBLASTOMA OF THE BASILAR PLATE OF THE SKULL AND ECCHORDOSIS PHYSALIPHORA SPHENO-OCCIPITALIS

SUGGESTIONS FOR DIAGNOSIS AND SURGICAL TREATMENT

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More and more tumors within the cranial chamber which hitherto have been considered inaccessible or inoperable are being radically attacked. Trying experiences with such a tumor—a chordoblastoma of the basilar plate—seem worth reporting, together with the pathologic study of a case of ecchordosis physaliphora spheno-occipitalis. Hints regarding the clinical diagnosis of both types of tumor and suggestions thought likely to facilitate and aid others to improve the operative procedure used are based on these experiences and on others recorded in the literature. The term chordoma is used to cover both types of tumor.

REPORT OF CASES

CASE 1.—*Chorodoblastoma of the basilar plate.*

History.—L. W., a medical student, aged 29, was first seen in the surgical division on May 18, 1933. His complaints were diplopia, partial weakness of the right internal rectus muscle, a sense of pressure in the head on changing position and numbness of the center of the face and forehead. Four and one-half years before admission he had had an attack of bilateral otitis media to which he dated his present difficulties. The attack, which was characterized by pain in both ears and impairment of hearing, was a sequel to a severe coryza. The tympanic membranes were said to have been tense and bulging, but although paracentesis was considered it was not carried out. About this time the patient noticed diplopia on looking to the extreme right. During the ensuing year there was a gradual increase in this complaint. Gaze straight ahead gave no difficulty, and at this time a squint was not noticed by other observers. The progression of symptoms took the form of increasing diplopia and a partial internal squint of the right eye.

Three years before admission the patient's wife noticed that when he drove an automobile his head was held rotated toward the right—obviously an attempt to provide for better fusion of images.

Two years before admission the diplopia became so much of a nuisance that the patient consulted an optometrist. Glasses were prescribed that gave a correction of the deviation of 6 degrees "inward." These lenses gave considerable temporary relief.

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Read before the Section on Nervous and Mental Diseases at the Eighty-Fifth Annual Session of the American Medical Association, Cleveland, June 13, 1934.

Twenty-one months before admission the patient noticed for the first time that diplopia was present on looking straight ahead. A further correction in glasses gave relief for the time. For one year before admission the squint had not been amenable to correction.

Seven or eight months before admission the patient first noticed a "sensation of pressure" in the region of the vertex of the skull. This occurred with such exertion as straining at stool, lifting weights or any rather sudden muscular activity. The patient stated that a few seconds after the inception of activity he felt a moderately severe, dull pain near the vertex of the cranium. This occurred in intermittent "waves" synchronous with the pulse, lasted perhaps two or three seconds and disappeared, being severe enough to obviate further effort. This continued with increasing severity up to the time of admission. The patient used enemas rather than expose himself to the effort of straining while defecating and curtailed all physical activities to avoid the pain accompanying exertion. The duration of the attacks became greater, and at times they merged into what might be called a continuous headache.

Six months prior to admission the patient was seen in the medical service of the hospital. At that time a diagnosis of an aneurysm of the basilar artery or an unlocalized tumor was considered (Dr. Paul C. Garvey). He was also seen briefly by me; erroneously, I did not believe there was enough in the history or observations to warrant making a ventriculogram. The results of all examinations were considered negative with the exception of (*a*) palsy of the right sixth nerve, (*b*) nystagmus, (*c*) a spinal fluid pressure of 220 mm. of water (the patient was very apprehensive and agitated) and (*d*) a 2 plus reaction for globulin (Pandy test).

Three months before admission dizziness was added to the sense of pressure and pain in the head as an accompaniment of exertion and change in position. At first this occurred only occasionally, coming on with sudden or gross changes in position. Later, however, it became increasingly easy to provoke, so that on admission it occurred with such trivial exertion as that entailed by coughing and laughing.

Three months before admission the patient began to notice emotional instability. He stated that during lectures he would "giggle" immoderately at witticisms that were not very funny. At motion picture shows minor tragedies evoked spells of weeping. Fifteen or twenty minutes were often required for the patient to bring himself under control. He appreciated the fact that the stimuli were not commensurate with the response but stated that he had no control over the response.

One month before admission occurred the first appearance of hypesthesia affecting the four upper central teeth. It was stated that the sensation resembled that of partial anesthesia with procaine hydrochloride accompanied by a vague feeling of pain or "irritation." At about this time the forehead, nose and both sides of the face began to feel numb. The sensation was described as resembling that produced by wax or lather dried on the face; likewise, a sense of "stiffness" of the facial muscles appeared. All these symptoms—the hypesthesia of the face and teeth and the sense of stiffness of the facial muscles—increased in extent up to the time of admission. From the first they were chiefly subjective phenomena apparently, since the patient repeatedly examined himself for appreciation of pinprick and light touch without discovering impairment.

Three weeks before admission the patient began to have moderate dysarthria. Apparently this was allied to pharyngeal and lingual muscular weakness or fatigue. The patient stated that after four or five minutes his "tongue became tired," his speech thickened and it became difficult to talk. This condition persisted.

For about three weeks the patient had suffered from stiffness of the neck. Turning the head to the right or left gave pain. He had slept with his head "centered" and had avoided rotation of the head as much as possible.

Two or three weeks before admission the patient noticed some weakness of both arms and both legs affecting the two sides equally. This was not marked, but combined with the dizziness previously mentioned it made him unsteady or insecure while walking and was responsible for a sense of fatigue after relatively slight exertion.

Neurologic Examination.—General Appearance: The patient was well developed and well nourished and lay quietly on the examining table in no apparent pain or distress. He was intelligent and cooperated well. The answers were at times given at some length, especially toward the end of the examination, and occasionally speech was somewhat thick. The hair was coarse and of normal male distribution. There was no increase in perspiration; the skin was warm, moist and of normal texture. The head was of normal size and shape; there were no dilatation of the veins, exostoses, abnormal pulsations or tenderness on percussion.

Sudden shifts in position, passive or active, evoked pain in the muscles of the neck. There was no real rigidity. Motions were carried out in normal arcs.

Striae appeared over the deltoid region, on the under surface of the upper part of the arms and on the flanks bilaterally. These were exactly similar to those seen in gravid women. The patient stated that they had been present since the age of 12 or 13, at which time he was obese.

Squint was present. The patient ordinarily kept the right eye closed, with a resultant inclination of the head toward the left.

Cranial Nerves: The olfactory nerves were normal. An examination of the optic nerves and their functions revealed that the visual acuity was not grossly impaired. The fields were intact in tests for form and color. Both fundi were hyperemic; the vessels bilaterally were rather larger than those of a normal person of this age and were overfilled. The disks were hyperemic and the margins were completely obliterated; they were covered by a fine, whitish exudate that made the lamina cribrosa invisible. A slight elevation of the nerve heads could be measured. Though these conditions were present bilaterally, they were somewhat more marked on the right side.

With regard to the functions of the oculomotor, trochlear and abducens nerves, the following observations were made: The pupils were of equal size but irregular. They were concentrically situated and reacted well to light and in accommodation. The right eye could not be deviated laterally past the midline. Fine nystagmus with the rapid component in the direction of gaze was elicited on deviation in any direction, vertical or horizontal. There was no ptosis or exophthalmos, although both eyes were prominent.

The trigeminal nerves were normal except for production of the subjective sensory changes already recorded. The facial and acoustic nerves were normal. The glossopharyngeal and vagus nerves were associated with the dysphagia and dysarthria already described. The interpretation of taste on the posterior third of the tongue was not impaired. The gag reflex was absent. The soft palate rose only moderately well, but there was no deviation from the midline. The spinal accessory nerves were normal. Involvement of the hypoglossal nerve was seen in the fact that the tongue tired easily with eating or prolonged conversation. There was no paresis, paralysis or tremor of the tongue.

Cerebrum: The patient had always been well oriented and had not noticed an impairment of memory. He believed that concentration was somewhat more difficult than formerly and was possible for a shorter period of time. After talk-

ing for several minutes on a subject requiring some mental exertion he was overcome by an impulse to fall asleep. This and emotional instability had been present for approximately three months. There was no history of uncinate seizures, hallucinations of taste or smell or dreamy states. No aphasia was present. There had been no convulsions. The patient noticed for the preceding two weeks some weakness of the arms and legs, but on examination of the muscles of the arms, legs, shoulder girdle, trunk and pelvis no weakness or inequality of function was manifest. There was no astereognosis, loss of muscle sense or apraxia. Sensation of touch, pain, temperature, pressure and changes in position was intact.

Cerebellum: Station was normal except for rotation of the head. The Romberg sign was negative. The gait was normal. Muscle tonus was normal. Finger-to-finger, finger-to-nose and heel-to-shin tests were performed with slight ataxia. Past-pointing was absent. Adiadokokinesis was absent.

Reflexes: Examination of the superficial reflexes revealed the corneal reflex to be present and equal on the two sides. The abdominal reflexes were reduced on the left and at times the upper left abdominal reflex could not be elicited. The scrotal reflex was diminished on the left. The Babinski, Oppenheim and Gordon reflexes were absent. Of the deep reflexes, the biceps, triceps and ankle jerks were present and equal on the two sides. The knee jerks could not be elicited and were known to have been absent for years. There was no patellar or ankle clonus.

Pituitary Symptoms: Neighborhood symptoms were generally absent except for the presence of headache and the appearance of the fundi. Glandular symptoms were generally absent except for the tendency to become fatigued easily and to drowse under the stimulus of continued mental exertion. Polyglandular symptoms were generally absent. The patient had one child living and well.

Summary of Positive Observations.—The subjective changes were: diplopia, four and one-half years; headache, seven months; dysphagia, six months; dizziness, three months; emotional instability, three months; difficulty in concentration, three months; hypesthesia of the face, one month; dysarthria, three weeks; "stiffness of neck," three weeks, and weakness of the arms and legs, two weeks. The general objective changes were: habitual rotation of the head to the left with the left eye only in use for ordinary activities, and striae over the upper part of the arms and the flanks. In the cranial nerves there were: swelling of both optic nerve heads of ½ diopter; complete paralysis of the right lateral rectus muscle; nystagmus, and absence of the gag reflex bilaterally showing involvement of the glossopharyngeal nerve. Slight ataxia was manifested in the finger-to-nose test. The upper abdominal reflex was absent on the left, and the lower abdominal reflex on the left was diminished. The scrotal reflex on the left was diminished, and neither knee jerk was elicited.

Diagnostic Impression.—The development of headache, numbness over both trigeminal nerve areas and early choked disks made a diagnosis of an intracranial tumor or chronic basilar arachnoiditis seem certain.

Laboratory Observations.—The usual examinations of the blood and urine gave normal results. An examination of the spinal fluid made six months prior to admission revealed a clear fluid under a water pressure of 220 mm.; the Pandy test was two plus; there were 6 lymphocytes per cubic millimeter, and the Wassermann reaction was negative.

Roentgen examination of the skull was first made in August 1932, nine months prior to admission. The films were at first considered to show a normal condition. Reexamination later disclosed a definite notch in the basilar plate, which is characteristic of chordoma. A reexamination of the skull by roentgen rays at the

time of admission revealed in addition to the notch in the basilar plate a forward bending of the posterior clinoid processes which was not present on the first examination.

Ventriculography.—On May 20, 1933, a burr hole was made in the right occipital region. The fluid in the ventricle was clear and under definitely increased pressure and was increased in amount. About 65 cc. of fluid and air was exchanged. Films showed a symmetrical dilatation of the lateral and third ventricles. The aqueduct of Sylvius and the posterior portion of the third and the fourth ventricle were outlined and were seen to be definitely elevated. The shadow of the fourth ventricle was definitely elongated as well as elevated (fig. 1).

Suboccipital Craniotomy.—On May 21 a wide suboccipital craniotomy was performed with the patient under anesthesia produced by 1 per cent procaine hydrochloride, 70 mg. per kilogram of avertin and a small amount of ether. I have

Fig. 1 (case 1).—A roentgenogram showing the elevation of the shadows of the third ventricle, the aqueduct of Sylvius and the fourth ventricle. The V-shaped notch in the basilar plate can be seen well only in plates viewed stereoscopically.

never encountered as great vascularity of the scalp and muscles in this region. Tapping of the lateral ventricles made little difference in the venous bleeding. When the dura was opened air from the ventriculography done on the previous afternoon was seen in the posterior cistern. The vermis of the cerebellum was not widened. The two cerebellar hemispheres were normal in size, color and consistency. The cerebellar tonsils were not displaced downward. The arachnoid over the posterior cistern was thin and normal in appearance. The right lobe of the cerebellum was retracted mediad, and the seventh and eighth cranial nerves were exposed. The arachnoid was grayish and thickened about them. Because of the symptoms referable to the fifth nerve the dissection was carried forward to expose the trigeminal root. In doing so a tumor ventral to the fifth, seventh and eighth nerves was encountered. This proved to be tough and relatively avascular. A specimen was taken for supravital staining and permanent section-

ing. After removal of the arch of the atlas the wound was closed in layers with interrupted silk sutures.

Postoperative Course.—During the next ten days there developed hypesthesia over the distribution of the left fifth nerve. Continued headache, fulness of the suboccipital decompression and continued elevation of the swelling of the optic nerve heads made it apparent that the cerebrospinal fluid block about the cerebral peduncles was unrelieved.

Pathologic Report.—A supravitally stained (neutral red) preparation showed the tumor to be composed of large round cells with a nucleus that nearly filled the cell. A diagnosis could not be made from the supravital preparations (fig. 2).

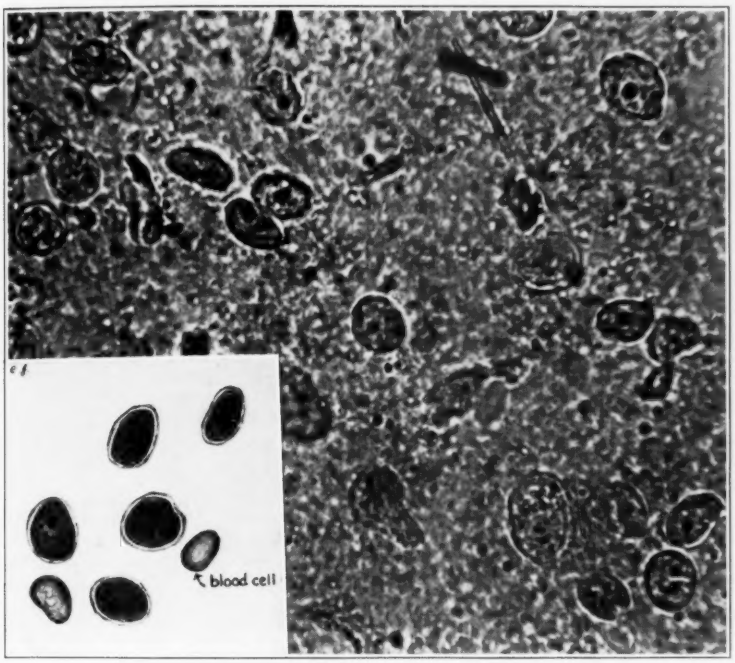

Fig. 2 (case 1).—A supravitally stained section of the chordoblastoma. Neutral red stain; magnification, × 960. The inset shows the comparative size of the red blood cells and the tumor cells.

In gross the tumor was unevenly lobulated reddish brown, tough and relatively avascular. There were a few medium-sized arteries coursing through its substance. There were no areas of degeneration in the tissue which could be removed by suction. Microscopically (hematoxylin and eosin stain) the tumor was made up of fairly large cells with a large nucleus and scanty cytoplasm. Intracellular and extracellular vacuolation gave the typical "foam" appearance. In addition there were several areas of larger mucoid-appearing cells which appeared to be not unlike primitive cartilage cells. Mitoses were observed in this type of cell. Intercellular bands of connective tissue were to be made out here and there. From sections a diagnosis of chordoblastoma, probably malignant, was made (fig. 3).

Second Operation.—In the hope of relieving the cerebrospinal fluid block the tentorium of the cerebellum was divided from the incisura to the right lateral sinus. This was done after reopening the right side of the cerebellar wound only. The cerebellum was retracted down and away from the tentorium. The cerebellopontile angle was again exposed, and more of the tumor ventral to the pons and the emergent fifth, seventh and eighth nerves removed. It soon became apparent that little could be done to deal adequately with this tumor without dividing these nerves, and for this permission had previously been denied.

Postoperative Course.—The impression gained following this procedure was that slight relief of the cerebrospinal fluid block had been obtained. However, the patient did not improve, and gradually difficulty developed in swallowing and

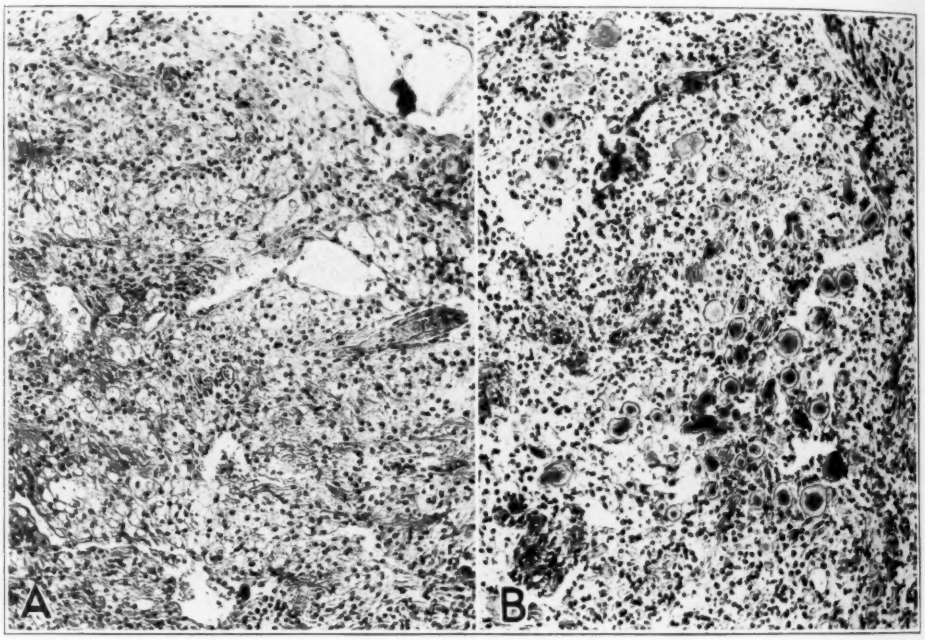

Fig. 3 (case 1).—Photomicrographs showing: *A*, areas of "foam cells," and *B*, young cartilage-like cells. Phosphotungstic acid-hematoxylin stain.

with speech. Vomiting became almost constant. It was not until the patient was moribund from vomiting and heightened intracranial pressure that permission for an attempt at radical extirpation was obtained.

Third Operation.—On September 9, three and one-half months after the first operation, the right half of the cerebellar wound was reopened with the patient under anesthesia produced by 1 per cent procaine hydrochloride and avertin (70 mg. per kilogram). The right cerebellopontile angle was reexposed, and the fifth, seventh and eighth nerves were divided. The anterior inferior cerebellar artery, which coursed along with the eighth nerve, was also divided (fig. 4). A slow, tedious task of extirpation of the tumor with pituitary rongeurs and the endotherm loop followed. The tumor was exceedingly tough. A few medium-sized arteries

coursed through it. When the extirpation had been completed it was possible to identify the stalk of the pituitary cephalad and the anterior rim of the foramen magnum caudad. These two structures marked the upper and the lower extent of the tumor. The right sixth nerve could not be identified at any time. The attachment of the tumor to the dura over the basilar plate was about 1.5 cm. in diameter.

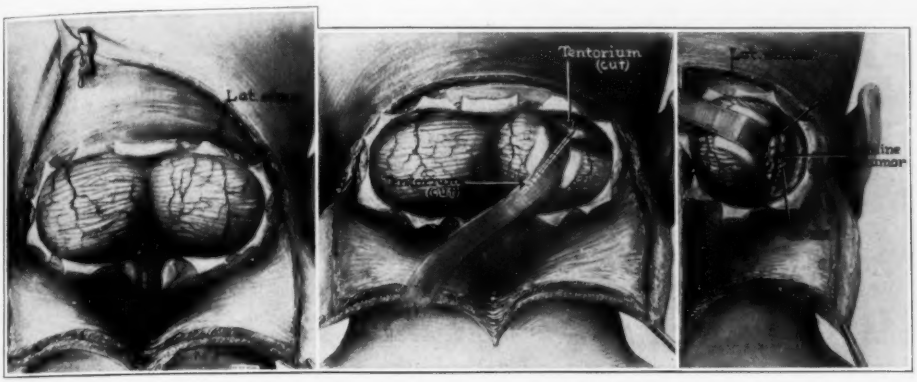

Fig. 4 (case 1).—Drawings illustrating the steps in the operative approach to the tumor.

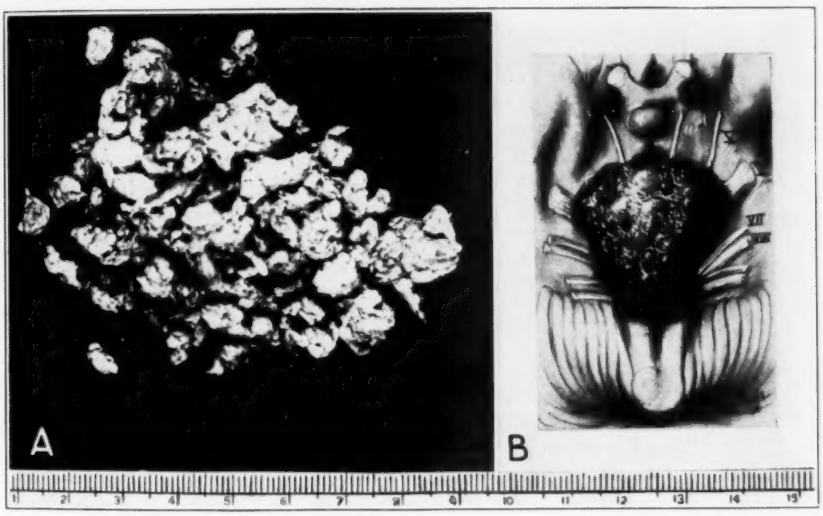

Fig. 5 (case 1).—*A*, a photograph of the specimen removed at operation; *B*, a reconstructed drawing showing the probable relation of the tumor to the brain stem and the cranial nerves.

This was thoroughly desiccated with the endotherm. The basilar artery was entirely freed from tumor tissue except at one small point where the tumor seemed to have enfolded it. It did not seem possible to remove this small cuff of tumor from around the artery. After painstaking hemostasis the wound was closed in layers with silk sutures (fig. 5).

Postoperative Course.—The patient regained consciousness in about four hours. A moderate wave of hyperthermia ensued which could be controlled by cold spongings. The bulbar signs which had been so pronounced gradually subsided. The eyelids on the right side were sutured together prior to the patient's discharge on the thirty-fifth postoperative day.

Four months after operation the patient was able to be up and about much of the time. He was able to walk with assistance. There was still a good deal of ataxia of both arms and legs. The cerebellar decompression remained flat. The choked disk subsided. The emotional outbursts of laughing persisted but to a lesser degree than formerly. Mentally he was bright and alert. One bout of headache and vomiting was experienced associated with a mild attack of grip.

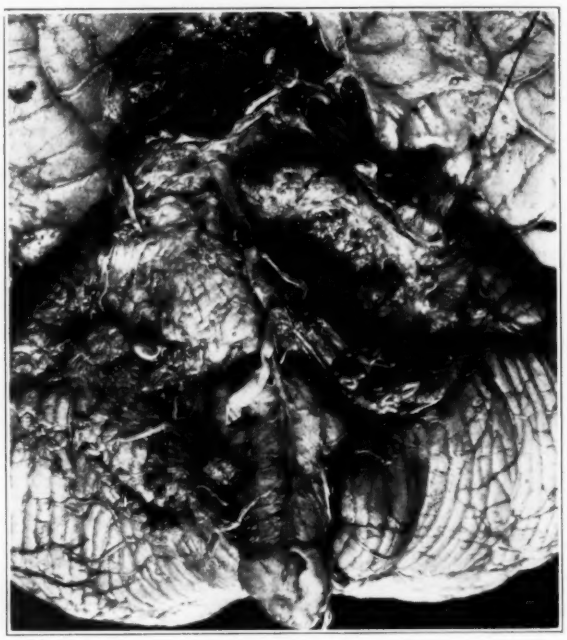

Fig. 6 (case 2).—The region of the brain stem, showing the gross deformity of the pons and brachium pontis from contact with the tumor.

At the end of six months the patient began to experience more headache and more frequent bouts of vomiting. The ataxia of the arms and legs became more marked. At the time of writing, about nine months following removal of the tumor, the patient is again confined to the hospital with evidences of recurrence of the tumor. There is now definite evidence of palsies of the left fifth, seventh and eighth nerves as well as more marked involvement of the left ninth, tenth and twelfth nerves. The decompression is full and tense. Headache is controlled by medication.

Case 2.—*Ecchordosis physaliphora spheno-occipitalis.*

History.—A. C., a painter, aged 45, admitted to the emergency ward on Feb. 19, 1934, for several weeks had complained of feeling "nervous and run-down."

Headache had been a minor complaint. Ataxia of the extremities, palsies of the cranial nerves and weakness of the extremities had never been noted. The past and family history were noncontributory.

On the day of admission to the hospital the patient had worked as usual until 4 p. m. when he went home because of headache. After a usual dinner he went

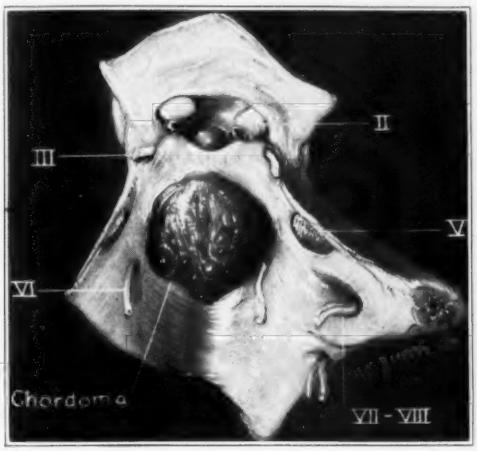

Fig. 7 (case 2).—A drawing of the specimen of ecchordosis physaliphora spheno-occipitalis showing its relation to the cranial nerves. The tumor before rupture was probably considerably larger than is shown.

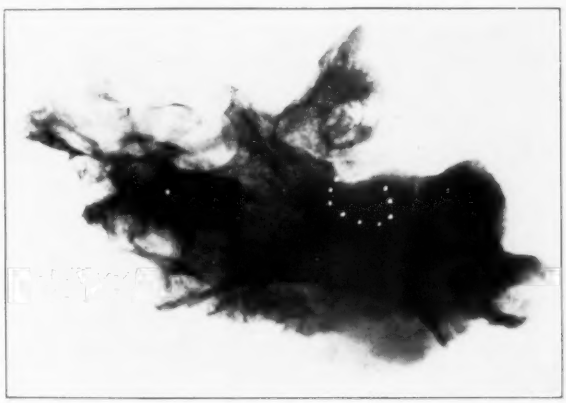

Fig. 8 (case 2).—A roentgenogram of the postmortem specimen showing the notch in the basilar plate produced by ecchordosis physaliphora spheno-occipitalis.

for a walk. A few moments later he was found lying in the street. In falling he had sustained an injury over the left temporoparietal region. Right hemiparesis and motor aphasia were noted. During the ensuing twenty-four hours the hemiparesis progressed and the patient grew comatose. Lumbar puncture disclosed blood-tinged fluid (300 red blood cells per cubic millimeter with a positive

Pandy reaction and under a pressure of 150 mm. of water. The history of injury and the progressive palsy on the right side gave rise to a suspicion of an extradural clot. A burr hole made over the left temporoparietal region failed to reveal a clot. Death occurred several hours later.

Autopsy.—Little of note was revealed aside from changes in the nervous system. On removal of the brain there was evidence of gross bleeding from a small aneurysm in the subarachnoid spaces about the brain stem. There was also a gross indentation deformity of the pons and brachium pontis on the left (fig. 6). This was due to a tumor arising from the basilar plate at the junction of the sphenoid and occipital bones. The capsule of the tumor was composed of thin connective tissue. Broken-down cellular, structureless débris made up the center of the mass. A diagnosis of ecchordosis physaliphora spheno-occipitalis was made (fig. 7).

Roentgen examination of the basilar plate post mortem showed a small but definite notch in the basilar plate which should have led one to suspect this diagnosis had premortem films been available (fig. 8).

DIAGNOSIS OF CHORDOMA OF THE BASILAR PLATE

It is doubtful if a diagnosis of chordoma of the basilar plate can be made from neurologic examination alone, although in case 1 a space-displacing mass ventral to the pons, an aneurysm, was suspected by the medical neurologist (Dr. Garvey).

In retrospect, however, it seems that the diagnosis should have been made readily, both from the roentgenograms and from the ventriculograms. Dr. M. C. Sosman [1] of Boston pointed out a characteristic V-shaped notch in the basilar plate as an almost certain sign. This deformity is undoubtedly due to destruction of the bone by a tumor. Late in the disease the entire basilar bone may be involved, as in a case reported by Eckel and Jacobs.[2] In addition there was a forward bending of the posterior clinoid processes which had progressed between the first and the last examination. Roentgen studies in the cases of three patients with aneurysm of the basilar artery have been made. In none of these did a V-shaped notch occur. In one instance a diffuse bowing of the plate was present similar to that seen in association with long-standing cerebellar tumors in children. The V-shaped notch is not present in all cases of intracranial chordoma, however. When the tumor arises in the floor of the sella turcica this structure may be greatly ballooned out or, as in the case reported by Alajouanine and his associates,[3] entirely destroyed. The elevation of the third ventricle and aqueduct of Sylvius, the pineal shadow and the deformation of the

1. Sosman, M. C.: Personal communication to the author.

2. Eckel, J. L., and Jacobs, W. F.: Malignant Spheno-Occipital Chordoma, J. Nerv. & Ment. Dis. **61**:471 (May) 1925.

3. Alajouanine, de Martel, Oberling and Guillaume: Chordome de la region sellaire: Considerations anatomiques et cliniques, Rev. neurol. **1**:1121 (June) 1930.

fourth ventricle demonstrated by means of a ventriculogram are unmistakable evidence of a tumor in the region of the upper part of the brain stem. This, coupled with multiple signs of involvement of the cranial nerves, places the lesion ventral to the pons.

A careful examination of the nasopharynx should be made. A number of these tumors reported in the literature have eroded the basilar plate and appeared in the nasal chamber. Hellmann [4] reported the case of a man, aged 30, with nasal obstruction from such a tumor. Spiess [5] reported the case of a patient with a tumor the size of a small hazelnut which he removed from the sphenoid bone, operating through the nose. Fabricius-Møller [6] reported the case of a boy, aged 16, with marked nasal obstruction. In Jelliffe and Larkin's [7] case the tumor had invaded the ethmoid cells.

A few cases have been reported of aberrant chordoma, such as over the occipital region of the skull, in both mandibles and in the postauricular tissues. In another case the tumor appeared in both the middle ear and the nasopharynx (Linck [8]). The few existing reports on surgical experiences with intracranial chordoma show that a tumor of the middle fossa is usually suspected. Cushing [9] reported two cases in which the records of the visual fields suggested pituitary adenoma. Biopsy showed the tumor to be a chordoma. Bailey and Bagdasar [10] reported a similar case from Cushing's clinic. Spiess also reported a case in which there was typical bitemporal hemianopia. Alajouanine, de Martel, Oberling and Guillaume reported a case in which a tumor of the right temporal fossa was suspected because of right exophthalmos, symptoms referable to the right trigeminal nerve, partial palsy of the right facial nerve and ocular palsy on the right. In addition roentgenograms of the skull showed what was thought to be calcification above the enlarged eroded sella turcica. The shadow of the pineal gland was displaced upward

4. Hellmann, K.: Ueber ein malignes Chordom des Nasenrachenraumes, Verhandl. d. Gesellsch. deutsch. Hals-, Nasen- u. Ohrenarzte, 1921, p. 111.

5. Spiess, Gustav: Tumor der Hypophysengegen auf endonasalem Wege erfolgreich operiert, München. med. Wchnschr. **58**:2503, 1911.

6. Fabricius-Møller, J.: Et tilfaelde af chordoma malignum med indvaekst i pharynx, Hospitalstid. **62**:849 (July 16) 1919.

7. Jelliffe, S. E., and Larkin, J. H.: Malignant Chordoma Involving Brain and Spinal Cord, J. Nerv. & Ment. Dis. **39**:1 (Jan.) 1912.

8. Linck, A.: Chordoma malignum, ein Beitrag zur Kenntnis der Geschwülste an der Schädelbasis, Beitr. z. path. Anat. u. z. allg. Path. **46**:573, 1909.

9. Cushing, H.: The Pituitary Body and Its Disorders, Philadelphia, J. B. Lippincott Company, 1912, p. 102, case 17.

10. Bailey, Percival, and Bagdasar, Dimitri: Intracranial Chordoblastoma, Am. J. Path. **5**:439, 1929. The bibliography presented by Bailey and Bagdasar is exceptionally complete; this makes it unnecessary to give here a more complete list of references.

and backward from its usual location. At operation no evidence of a tumor in that region was found. Autopsy disclosed a typically placed chordoma overlying the basilar plate and beneath the third ventricle and pons. The authors believed that it arose from the floor of the sella turcica.

The cases reported in the literature have been reviewed in an attempt to learn the relative frequency of symptoms and signs. The data are admittedly meager, and the following statements may have to be revised as time goes on: Palsies of the ocular nerves outweigh all others in frequency and date of onset; of these palsy of the sixth nerve is the most frequent. Other cranial nerve palsies, notably those of the trigeminal and vagus nerves, follow next in frequency. As the tumor grows, cranial nerve palsies may be bilateral. Symptoms of intracranial pressure may be ranked third in frequency. Symptoms referable to the optic nerves, including failing vision due to choked disks or changes in the fields, seem to rank fourth in frequency and date of onset. Symptoms of involvement of the pyramidal tracts rank next in frequency. Symptoms of cerebellar involvement are meager until late in the disease, and there is a surprising lack of symptoms referable to the facial and auditory nerves until late. Convulsions seldom occur. Sphincter disturbances do not occur until late. Polydypsia has not been reported as a symptom; neither have disturbances of the sleep cycle, gastro-intestinal bleeding or ulcerations.

The average period of time from the first symptom to death in the reported cases is two and one-fourth years. There are few data available regarding the response to irradiation. The patient in Cushing's second case lived five years after biopsy of the tumor. During this period the area of the tumor had been thoroughly irradiated.

SUMMARY

Chordoblastoma of the basilar plate of the skull and ecchordosis physaliphora spheno-occipitalis are tumors which seem to lend themselves to diagnosis and at least to palliative surgical treatment. The diagnosis rests on a combination of clinical and roentgen observations. Multiple palsies of the cranial nerves, notably of the abducens, trigeminal, optic, and glossopharyngeal nerves, which are often bilateral, signs referable to the pyramidal tract and at times cerebellar signs, in the presence of a roentgen demonstration of a V-shaped notch in the basilar plate and an elevation of the pineal shadow or of the third ventricle, the aqueduct of Sylvius or the fourth ventricle, strongly suggest the diagnosis. Particularly is this true in the presence of a tumor invading the nasopharynx without evidence of cervical metastases from carcinoma in that region.

Experiences with the chordoblastoma in case 1 suggest certain measures which in the future may assist others in dealing with this type of tumor. At a first stage operation a wide cerebellar decompression exposing the lateral sinus near the mastoid might well be done. The lateral third or half of the cerebellar lobe on the side of the greater palsies of the cranial nerves probably should then be removed. A next important step would seem to be section of the tentorium of the cerebellum from the incisura to the lateral sinus on the side of the resected cerebellum. Without this step it would be difficult to gain exposure of the upper end of the tumor adjoining the posterior clinoid processes.

A second stage procedure would seem warranted owing to the tedious, time-consuming process of piecemeal extirpation of the tumor with small rongeurs or the endotherm loop. It seems unlikely that a tumor of any particular size could be dealt with without section of the fifth, seventh and eighth nerves. Such section gives one a view of the branches of the basilar artery coursing over the dorsal surface of the tumor. The attachment of the tumor to the basilar plate should be thoroughly desiccated with the endotherm. In spite of a most painstaking surgical removal one might well expect recurrences of a chordoblastoma (case 1) from the point of origin in the basilar plate. The benign ecchordosis physaliphora (case 2), however, should be cured by this procedure.

ABSTRACT OF DISCUSSION

Dr. John L. Eckel, Buffalo: I shall limit my remarks to the origin, symptoms and histopathology of this rare type of tumor and leave the surgical discussion to Dr. Gardner. About ten years ago I had the opportunity to study a patient with such a tumor both ante mortem and post mortem.

Chordoma arises from remains of the primitive chorda dorsalis which normally undergoes degeneration except for small rests known as the nuclei pulposi which are found in the center of the intervertebral disks. Frequently remains may also be found at the junction of the sacrococcygeal bones and at the base of the skull at the spheno-occipital synchondrosis. As a result of some irritation the cells of these rests or remains may overgrow, resulting in the formation of a tumor. In the greater number of cases the tumor is small and benign and produces no symptoms, but occasionally it becomes large and may undergo malignant changes and produce serious symptoms and death.

The tumor may present itself in the neck, at some other point along the spine or at the base of the skull. A growth at the base of the skull may project itself in any direction, that is, laterally, backward or forward, and the symptoms it produces depend largely on the direction which it takes. If it extends backward or laterally multiple cranial nerve palsies result, and if forward, it may extend into the back of the nose. The process is long drawn out, few of the tumors running a course of less than from two to four years before death, even without operation. Owing to the tendency to undergo malignant degeneration and thus to invade surrounding tissue the earlier the diagnosis the better the outlook for surgical treatment. In the case I observed the course was two years and nine months; the tumor had its origin from the basilar bone and produced, in addition to some cranial nerve palsies, complete paralysis from the neck down.

With reference to the V-shaped notch in the basilar bone, described by Dr. Van Wagenen as a diagnostic feature, I believe that this notch may be absent in many cases in which the tumor does not project in the same direction as it did in his case. The only accurate method of diagnosis of the type of tumor is by biopsy.

The histopathologic examination usually reveals a tumor having a homogeneous matrix containing the tumor elements. The cells do not show any orderly arrangement as a rule, and they vary in size, shape and content. Vacuolation is a striking feature. The cells at the periphery are the most characteristic. Many of the cells become elongated, with nuclei in the larger, bulbous end, resulting from the vacuoles pushing them to one side. Many thus give a so-called signet-ring or leather bottle appearance. The center of most of these tumors of long standing has undergone necrosis.

Owing to the tendency of these tumors to become malignant, the earlier the diagnosis and attempted removal the better the prognosis for recovery.

Dr. W. James Gardner, Cleveland: Dr. Van Wagenen's paper recalled the case of a patient whom I first saw some months ago and whose case resembles closely the two reported on today. My patient is a man, aged 62, in whom progressive paralysis of the cranial nerves has developed during the past year. This involves the nerves on both sides from the fifth to the twelfth, inclusive. The basilar plate cannot be seen well in the roentgenograms, which precludes the determination of the presence or absence of a depression. However, in view of Dr. Van Wagenen's experience I believe that an operation should be attempted in this case.

The author is to be commended for his efforts to deal with this formerly hopeless lesion. I predict that, as is usually the case when a satisfactory method of treatment is devised, the lesion under discussion will prove to be more prevalent than it is now generally conceded to be.

Dr. Alfred W. Adson, Rochester, Minn.: I have operated on two patients with a tumor arising from the clivus Blumenbachii, and in neither case was the exact condition recognized before operation. One patient presented symptoms of a pituitary tumor. The tumor had elevated the dura in the region of the left anterior clinoid process. When I split the dura, pinkish cartilaginous material exuded, and I continued to curet away this tumorous material until I had a large hole in the body of the sphenoid; I thought I had removed all the tumor. To my surprise the pathologic examination revealed chordoma. Some two years later the patient presented symptoms which indicated that the tumor had extended to the other side. The patient is still living, although greatly incapacitated. The second patient presented symptoms of a tumor of the cerebellopontile angle, the growth displacing the pons dorsally and to the left. Cerebellar exploration revealed that the tumor was situated extradurally and that it arose from the clivus Blumenbachii.

In a third case the patient presented symptoms of a tumor of the spinal cord with erosion of the second and third cervical vertebrae and slight erosion of the first. I suspected this tumor to be a neurofibroma since I was able to remove it completely. I was surprised to learn, however, that it was a chordoma. It differed from the tumor in the previous two cases, as it was encapsulated and was removed in lobules.

At the clinic my assistant and I have had ten cases of sacrococcygeal chordoma. Two of the patients are still living, one nine years and the other eight months after operation. The others died from eight months to seven years after operation. It is my impression that all these tumors are malignant and some more malignant than others.

In cases of sacral chordoma I believe one is justified in opening the dorsum of the sacrum and in removing as much of the tumor as possible, since removal of the tumor tends to inhibit growth into adjacent bony structures and relieves pain to a certain degree. It is possible, too, that treatment with roentgen rays may retard the growth of the more vascular tumors.

Naturally we studied the roentgenograms following operation in the two cases in which the tumor arose from the clivus Blumenbachii, but even then we were not able to demonstrate the V-shaped indentation in the basilar plate to which Dr. Van Wagenen has called attention.

I question whether it is possible to remove all the growth in cases of cranial chordoma or of chordoma in any situation; because of the slow progression of symptoms, however, I agree with Dr. Van Wagenen that one is justified in removing at least as much of the tumor as possible in order to prolong life.

CEREBROSPINAL HYDRODYNAMICS

VI. CORRELATIONS OF THE PRESSURE OF THE CEREBROSPINAL FLUID WITH AGE, BLOOD PRESSURE AND THE PRESSURE INDEX

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It is the purpose of this paper to present a statistical analysis of certain correlations of the pressure of the cerebrospinal fluid in the human being as determined in previous clinical studies of cerebrospinal hydrodynamics.[1]

TABLE 1.—*Correlations of the Pressure of the Cerebrospinal Fluid with Age, the Arterial Blood Pressure and the Index of Fall of the Cerebrospinal Fluid Pressure After Lumbar Drainage*

Series No.	Series	N	Range	Mean	σm	rep	P.E.rep	P.E.r0	C.R.rep
1	C.P.	200	42-228	151.5	1.79				
						+0.060	0.047	0.048	0.88
2	Age	200	16- 56	39.06	8.32				
3	B.P.s	120	68-220	121.9	29.2	+0.306	0.054	0.062	3.72
4	B.P.d	120	40-120	83.40	14.7	+0.308	0.058	0.065	3.54
5	P.I.	200	0.05-0.78	0.325	0.132	−0.532	0.034	0.048	9.02

B.P.d indicates the diastolic blood pressure; B.P.s, systolic blood pressure; C.P., the pressure of the cerebrospinal fluid in millimeters of water with the patient at rest in the horizontal position; C.R.rep, the critical ratio of the appurtenant correlation coefficient; N, the number of cases in a series; P.E.rep, the probable error of coefficient of the correlation rep; P.E.r0, the probable error of the control coefficient of zero correlation; P.I., the pressure index—the ratio of the number of cubic centimeters of spinal fluid (range 15 to 40 cc.) drained in an individual case to the resultant fall of the cerebrospinal fluid pressure in millimeters of water; rep, the coefficient of correlation of a series of data with the distribution of coincident readings of cerebrospinal fluid pressure; σ, the standard deviation of the mean of a series of observations.

MATERIAL AND METHOD

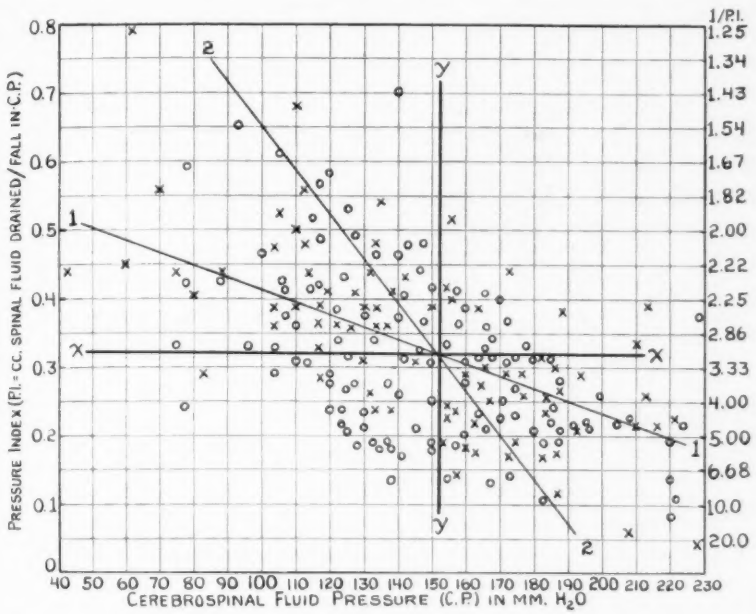
The patients ranged in age from 16 to 48. The basic pressure of the cerebrospinal fluid in each case was determined after from fifteen to sixty minutes of continuous observation with the patient at complete rest in the horizontal position. The pressure index (the ratio of the number of cubic centimeters of spinal fluid removed to the resultant fall of cerebrospinal fluid pressure in millimeters of water) was calculated in each instance for a drainage confined to 15 to 40 cc. of fluid, since only within this range does the index of an individual patient remain relatively constant.[2] Seventy-seven of the two hundred subjects were patients

From the Baltimore City Hospitals, and Phipps Psychiatric Clinic, Johns Hopkins Hospital, Baltimore.

1. Masserman, J. H.: Cerebrospinal Hydrodynamics: IV. Clinical Experimental Studies, Arch. Neurol. & Psychiat. **32**:523 (Sept.) 1934.

2. Masserman, J. H.: Cerebrospinal Hydrodynamics: V. Studies of the Coefficient of Volume Elasticity of the Human Ventriculo-Subarachnoid System, J. Comp. Neurol. **61**:543 (June) 1935.

with dementia paralytica, but as the constants for this group did not differ significantly in any respect from the corresponding data for control patients with no demonstrable lesions of the central nervous system, the observations on the two groups were combined in calculating the grand means and the coefficients of correlation for the entire series. The constants, according to standard statistical technic, were considered significant only when their critical ratios exceeded 3.5.



Graphic analysis of the correlations of the cerebrospinal fluid pressure and the corresponding pressure index in 200 cases. Individual observations on control patients are indicated by circles; observations on patients with dementia paralytica are indicated by crosses. The mean cerebrospinal fluid pressure for the entire group (line *y-y*) is 151.7 ± 1.79 mm. of water, and the mean pressure index (line *x-x*) is 0.325 ± 0.344. The coefficient of correlation between these two values is $r = -0.532 \pm 0.034$, the regression formulas being:

Mean pressure index (line *1-1*) = 0.609 — (cerebrospinal fluid pressure × 0.00188)

Mean cerebrospinal fluid pressure (line *2-2*) = 200.6 — (pressure index × 150)

The regression line (*1-1*) may be utilized clinically to estimate the amount of diminution in cerebrospinal fluid pressure to be anticipated in an individual case following the removal of a given amount of spinal fluid. For example, the abscissa of the pressure index corresponding to a cerebrospinal fluid pressure of 80 mm. of water is 0.45, so that following the removal of 20 cc. of spinal fluid from a patient with this initial tension, the expected drop in the subarachnoid pressure will be 20/0.45, or about 44 mm. of water. To facilitate this computation, the amount of fluid removed can be multiplied by the corresponding reciprocal of the pressure index scaled at the right of the chart, thus: 20 × 2.22 = 44 mm. of water. In approximately two thirds of the cases, the deviation, according to the formula $\sigma_{xy} = \sigma_x \sqrt{1 - r^2}$ will be within about a fourth of the result, or in the example, 44 ± 11 mm. of water.

RESULTS

From the statistical analyses presented in the table and chart these conclusions may be drawn:

1. There is no significant correlation between age alone and cerebrospinal fluid pressure in the human being (table, series 1 and 2).

2. There is a small but significant parallel covariance between both the systolic and the diastolic arterial blood pressure and the pressure of the cerebrospinal fluid (table, series 3 and 4).

3. There is a definite negative correlation (-0.532 ± 0.034) between the cerebrospinal fluid pressure and the pressure index, so that in the majority of both normal patients and those with dementia paralytica, the higher the initial pressure the greater will be its fall per cubic centimeter of spinal fluid removed at lumbar puncture.

TUMORS IN THE REGION OF THE PINEAL BODY

A CLINICOPATHOLOGIC REPORT OF THREE CASES

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Though the literature on the pineal body and its tumors is extensive, cases occasionally occur which are unique and for this reason are of universal scientific interest. Three such cases, all of tumor in the region of the pineal body—a mixed tumor, an astroblastoma and a calcified meningioma or psammoma—are reported here clinically and pathologically. According to my knowledge, such conditions in the pineal body have not yet been described.

REPORT OF CASES

CASE 1.—*A Mixed tumor of the pineal body with teratoid features in a boy aged 14. The clinical symptoms were due largely to pressure on the quadrigeminal plate.*

History.—The patient was admitted to the Cook County Hospital on Nov. 14, 1933, with a complaint of occipital headache, diplopia, vomiting and gradually developing stupor of five days' duration. The patient had sustained a fall prior to the onset of the foregoing symptoms (the information was obtained before death).

Examination.—The patient was somewhat stuporous; when questioned he responded promptly but in a silly manner; his attention was sustained poorly. There were fine choreiform jerks of the hands and arms at irregular intervals. The findings in the chest, abdomen and genitals were essentially normal. The temperature was 98.6 F., the pulse rate was 60, and the respiratory rate was 20. The pupils were moderately dilated, round and equal but did not react to light; the reaction in accommodation was questionable. The right eye was held diverged but moved inward with conjugate movement to the left. Rapid, lateral nystagmus was brought out by movements of the eyes to the right and left and vertical nystagmus was noted on attempting to look down. There was inability to raise the eyes above the horizontal level. The corneal reflexes were markedly diminished. Ophthalmoscopic examination revealed engorged and hyperemic disks but no definite papilledema. The tongue had a slight tremor but did not deviate from the midline. The neck was slightly rigid. Brudzinski's and Kernig's signs were not present.

Reflexes: The reflex in the left upper quadrant of the abdomen was more lively than that in the right, but there was absence of the reflexes in the lower

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Read before the Chicago Neurological Society, Nov. 15, 1934.

From the Pathology Laboratories of the Cook County Hospital (Dr. R. H. Jaffé, Director) and the Division of Neuropathology (Dr. G. B. Hassin), University of Illinois College of Medicine.

quadrants. All tendon reflexes were exaggerated in the upper and lower extremities, and suggestive Babinski and Chaddock signs were obtained on the right. The muscle power was good throughout, and sensibility, including the position sense, was intact.

Laboratory Findings: The spinal fluid was clear and under normal pressure; the Pandy test was negative, and there were 10 lymphocytes per cubic millimeter (repeated puncture at a later date showed 235 lymphocytes); the Wassermann reaction of the fluid was negative, and the sugar content was 79 mg. per hundred cubic centimeters. The hemoglobin content was 75 per cent; the red blood cell count was 4,610,000 and the white blood cell count was 11,000, with a differential

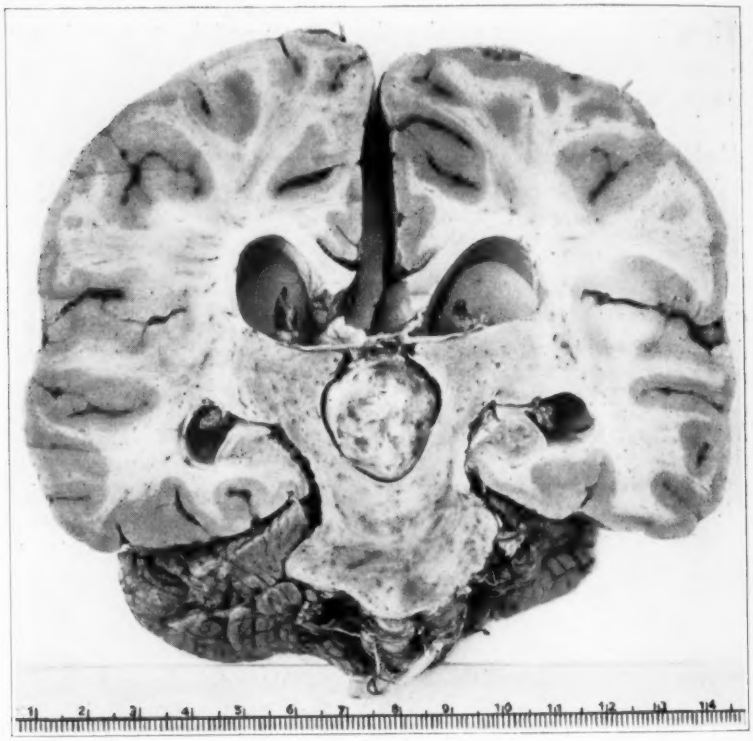

Fig. 1 (case 1).—Photograph showing the encapsulated tumor of the pineal body occluding the markedly dilated cerebral aqueduct.

count of 73 per cent polymorphonuclear cells, 22 per cent lymphocytes and 5 per cent monocytes. The urine was normal.

Course.—The patient remained stuporous and exhibited continuous spasmodic, purposeless, incoordinated movements of the upper extremities. There were no signs of meningeal involvement. The temperature rose to 103 F., and the patient died six days after he was admitted to the hospital.

Clinical Diagnosis.—Epidemic encephalitis was suggested, especially because of the recent occurrence of an epidemic of this disease.

Necropsy (Dr. Jerry Kearns).—The examination was limited to the head. The convolutions of the brain were flattened. The meninges were thin and slightly

injected, and the vessels at the base were thin-walled and patent. There was no evidence of an exudate or hemorrhages.

Macroscopic Observations: The brain, cut serially in coronal sections, contained an egg-shaped tumor 2 cm. in width and 3 cm. in length. It was light gray, was studded with cystlike cavities (fig. 1) and entirely replaced the pineal body, which was missing. The tumor was well encapsulated and could easily be

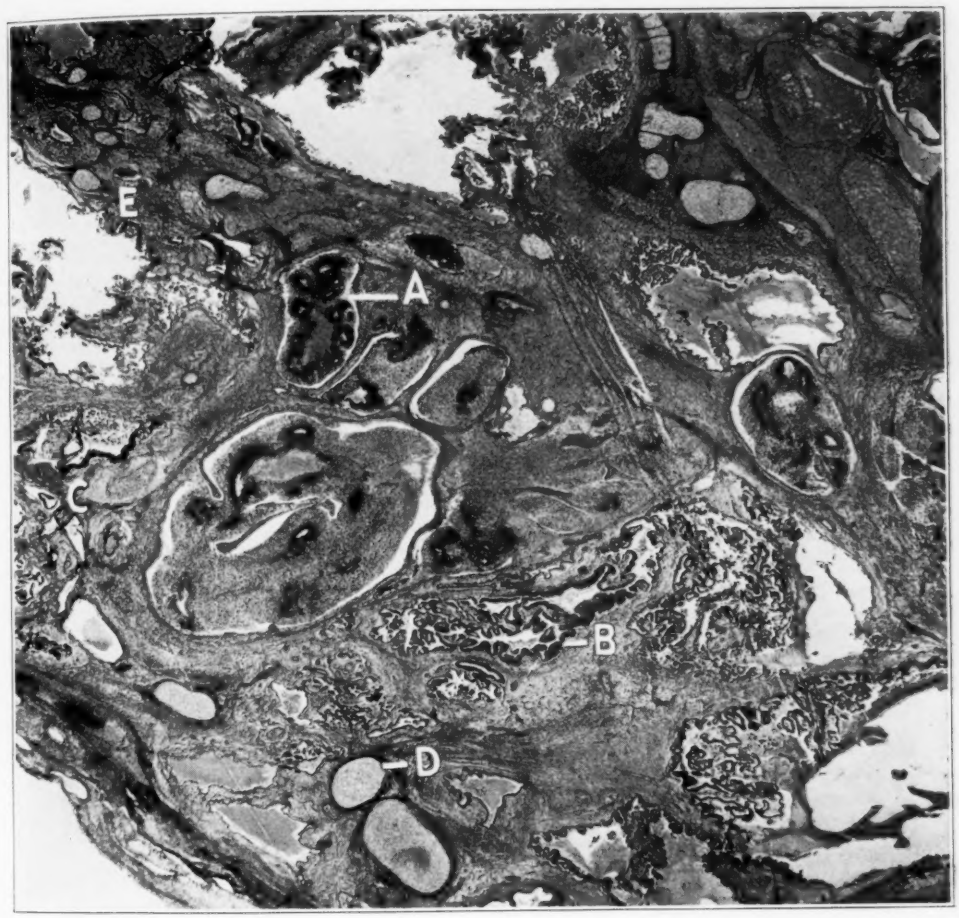

Fig. 2 (case 1).—A section of the tumor showing the different structures: *A* indicates neuro-epithelial tissue; *B*, the papillomatous tissue of the choroid plexus; *C*, pigmented epithelial cells; *D*, cartilage cells, and *E*, cystic formation. Higher magnifications of the section are shown in figures 3, 4 and 5. Van Gieson's stain; low magnification.

separated from the adjacent brain tissue. Below, it almost completely occluded the aqueduct of Sylvius, and rostrally it extended as far as the posterior portion of the third ventricle. Caudad, the anterior quadrigeminal plate was compressed as far as the anterior edge of the cerebellum, and above, the splenium of the

corpus callosum was reduced to a thin plate. The third and lateral ventricles were considerably dilated.

Microscopic Observations: In general, the tumor was cystic and composed of mesenchymal tissue in the form of hyaline cartilage surrounded by connective tissue, choroid epithelium, neuro-epithelial tissue and pigmented epithelial cells (fig. 2).

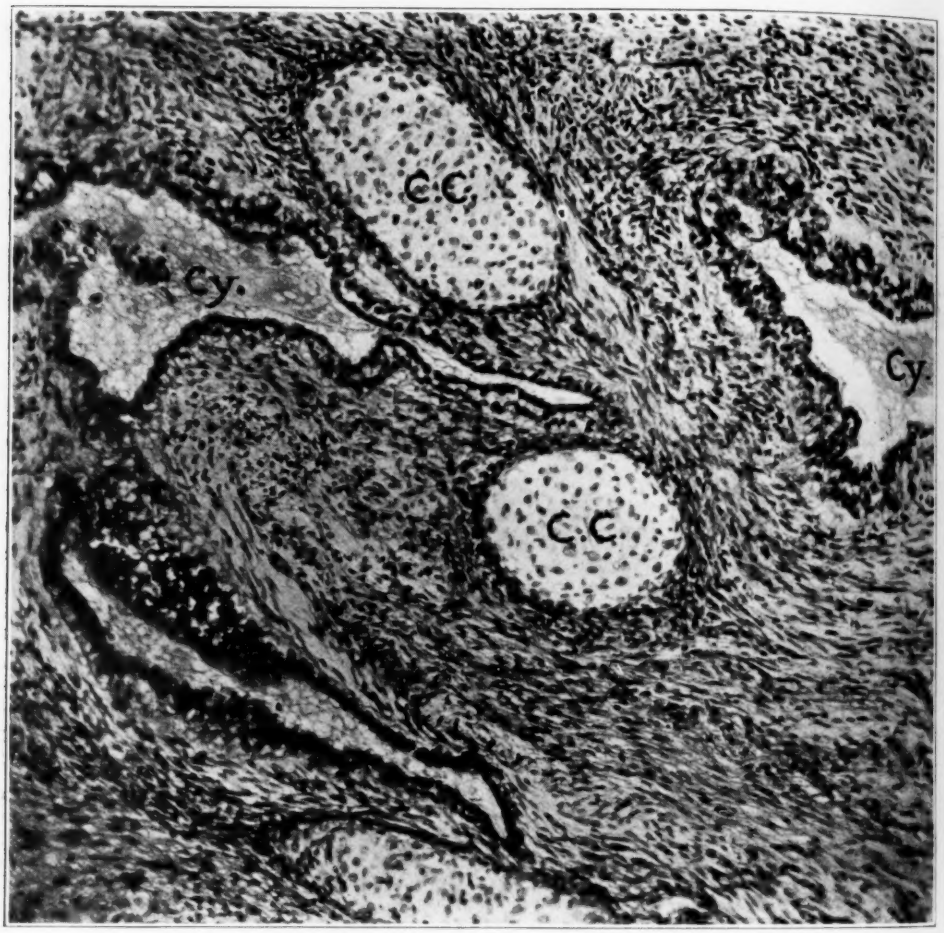

Fig. 3 (case 1).—A higher magnification (× 300) of the section of hyaline cartilage (*C.C.*), cells and the cysts (*Cy.*) lined with cuboidal epithelial cells shown at *D*, in figure 2. Van Gieson's stain.

The outer surface of the tumor was surrounded by a layer of loose, fibrillary connective tissue. This connective tissue contained elongated, oval or round nuclei with fine and coarse chromatin granules and small laminated layers of calcareous concretions. The loose stroma contained many dilated blood vessels and spaces filled with protein coagula and occasionally with red blood cells. Sharply demarcated islands of well developed hyaline cartilage cells were occasionally present near

cystlike structures which were lined by a single layer of cuboidal epithelial cells and were surrounded by connective tissue (fig. 3). Extending from the outer fibrillary connective tissue layer were cauliflower-like, outbranching villi with many collaterals, some of which were broad and others narrow. The central core of these villi contained thin-walled blood vessels and a fibrous connective tissue. In some villi the epithelial cells were arranged in a single layer; in others they were

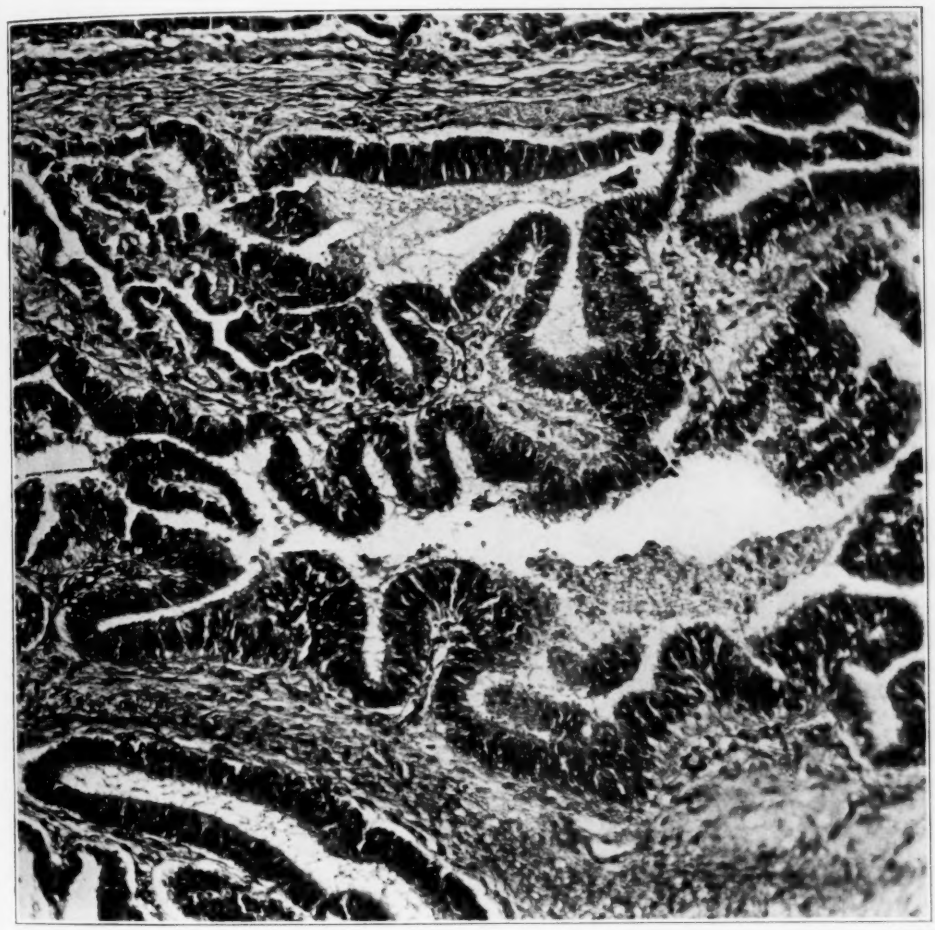

Fig. 4 (case 1).—A higher magnification (×300) of the area seen at *B* in figure 1, showing the villous structure of the papillomatous tissue of the choroid plexus with a connective tissue core. Bailey's ethyl violet-orange G stain.

two or three layers deep and tall and columnar. The nuclei were centrally placed, and in shape varied from round to oval. The cytoplasm was lightly stained and finely granular. Blepharoplasts were not demonstrable in these villous structures (fig. 4).

Other areas contained primitive spongioblasts, oval and cylindric, with chromatin granules in the nuclei. These cells were arranged about clear spaces in the form

of rosettes. The lining of the spaces was formed by the inner surface of the primitive spongioblastic cells. The rosettes simulated the central canal of a developing neural tube. Occasionally the cells were one layer deep with a distinct internal and external limiting membrane, but more often the cells were several layers deep and the external limiting membrane was wanting (fig. 5). The rosettes were located closely together and were concentrically arranged. The canals were

Fig. 5 (case 1).—A higher magnification (× 300) of the area seen at *A* in figure 1. *X* indicates true rosettes simulating the central canal of the developing neural tube. Bailey's ethyl violet-orange G stain.

lined by a distinct cuticular membrane which contained numerous minute, dark-staining, round rod-shaped bodies resembling blepharoplasts and were seen best when stained with Bailey's neutral ethyl violet-orange G stain [1] and Fincher's modi-

1. Bailey, P.: New Principle Applied to Staining of Fibrillary Neuroglia, J. M. Research **44**:73, 1923.

fication of Hortega's silver carbonate stain.[2] From the lining membrane of the canals minute cilia could be seen extending into the lumens (fig. 6 *B*). The outer ends of the cells of the rosettes were irregular and tapered off in the surrounding tissue. There were also groups of primitive spongioblasts massed together, but with no signs of organization. The foregoing features are characteristic of neuroepitheliomas as repeatedly described by Bailey and Cushing. Scattered in other places were single layers of columnar epithelial cells with round nuclei and an abundant cytoplasm forming the lining of large cavities. The inner surface of these cells contained numerous rod-shaped to needle-shaped bodies of melanotic

Fig. 6 (case 1).—Magnification under oil immersion of the area seen at *X* in figure 5. *A* indicates the blepharoplasts (inserted, as they were, out of focus) and, *B*, cilia extending into the lumen. Bailey's ethyl violet-orange G stain; × 1200.

pigment, arranged serially and parallel to the long axis, but the base was free from pigment. Mitotic figures were not present.

Microscopic examination of the remaining parts of the brain and meninges revealed no abnormalities.

Comment.—The mass in this case may be classed as a mixed tumor of the pineal body with teratoid features, a combination of neuroepithelioma, papilloma choroideum, pigment cells and cartilage. Though

2. Fincher, E. F.: Hortega's Silver Carbonate Modification, Am. J. Cancer **16**:4, 1932.

some cell structures, for instance those of neuro-epithelioma, have been described from time to time in different regions of the brain (Bailey,[3] Naesbund,[4] Bucy and Muncie [5]), in the retina (Flexner and Wenterstainer) and in the spinal cord (Schlapp; Rosenthal), they were not described in the pineal body. Tumors of the pineal body composed of ependymal and ependymoblastic cells arranged about clear spaces have been recorded as neurogliomas by Businco,[6] Rohrschach,[7] Schmincke,[8] Derman and Kapelowitsch [9] and Pappenheimer, [10] while Lereboullet, Maillet and Brizard [11] reported a neuro-epithelial glioma. The tumor, which in some features much resembled that in my case, consisted of epithelial formations in the form of pseudoglandular tubes lined with single layers of cylindric epithelial cells which formed papillary vegetations.

Papilloma or tumor of the choroid plexus is another relatively uncommon intracranial tumor. The incidence is only about 0.5 per cent of all intracranial neoplasms. In the cases recorded (Boudet and Clunet,[12] Davis and Cushing,[13] Van Wagenen,[14] and Hall and Fentress [15]) the papilloma was frequently located in one of the cerebral ventricles, especially in the lateral ventricle, but occurrence in the pineal body, as in my case, has never been reported.

In its papillomatous character the tumor of the choroid plexus bears a close resemblance to the rare forms of papillary ependymoma. Morphologically, the choroid plexus and the ependymal cells have the same

3. Bailey, P.: Further Remarks Concerning Tumors of the Glioma Group, Bull. Johns Hopkins Hosp. **40**:354, 1927.

4. Naesbund, J.: A Study of Neuroepithelioma Gliomatosum, Upsala läkaref. förh. **31**:193, 1926.

5. Bucy, P., and Muncie, W. S.: Neuroepithelioma of the Cerebellum, Am. J. Path. **5**:157, 1929.

6. Businco, A.: Cystic Neuroglia of Pineal Gland, Tumori **7**:163, 1921.

7. Rohrschach, H.: Zur Pathologie und Operabilität der Tumoren der Zirbeldrüse, Beitr. z. klin. Chir. **83**:451, 1913.

8. Schmincke: Ueber die Teratome der Zirbeldrüse, München. med. Wchnschr. **61**:2043, 1914.

9. Derman, G. L., and Kapelowitsch, M. A.: Virchows Arch. f. path. Anat. **273**:657, 1929.

10. Pappenheimer, A. M.: Neurogliomaependymoma of Pineal Body, Virchows Arch. f. path. Anat. **200**:122, 1910.

11. Lereboullet, Maillet and Brizard: Un cas de tumeur de l'épiphyse, Bull. Soc. de pédiat. de Paris **19**:116, 1921.

12. Boudet and Clunet: Arch. de méd. expér. et d'anat. path. **22**:379, 1910.

13. Davis, L., and Cushing, H.: Papillomas of the Choroid Plexus, Arch. Neurol. & Psychiat. **13**:681 (June) 1925.

14. Van Wagenen, W. P.: Papillomas of the Choroid Plexus, Arch. Surg. **20**: 199 (Feb.) 1930.

15. Hall, G. W., and Fentress, T. L.: Papilloma Chorioideum with Diffuse Central Nervous System Metastasis, J. Neurol. & Psychopath. **14**:108, 1934.

origin from the primitive spongioblasts, their differentiation occurring later. The true ependymal cells lie adjacent to a dense layer of fibrillary glia or subependymal glia. The tuft cells of the choroid plexus rest on a connective tissue stroma which contains a rich network of blood vessels. In embryonic life the choroid cells are ciliated and contain blepharoplasts. In the human adult the tuft cells have no blepharoplasts, which are present in the adult ependymal cells as well as in the neuro-epithelial tissue (Mallory [16]). This fact serves as a means of differentiating these two structures. The same holds true in distinguishing papillomas of the plexus from papillary ependymal tumors, as emphasized by Saxer,[17] Bielschowsky and Unger,[18] Davis and Cushing [13] and others. Saxer and later Cushing and Davis stressed that the core of a tumor of the plexus is composed of connective tissue and small blood vessels, whereas the core of an ependymal papilloma is formed by subependymal glia. The presence of mitochondria in the epithelial cells covering the villi has also been pointed out. The granules described about the nucleus of these tuft cells may be assumed to be granules of the nature of mitochrondria since they failed to stain by the ethyl violet-orange G method of Bailey. These points of differentiation, like the absence of blepharoplasts and the presence of connective tissue with small blood vessels in the papillary core together with the presence of mitochondria, show precisely that the nature of this tissue is that of a papilloma of the choroid plexus.

Pigment, according to Uemura,[19] is normally present in the pineal body. Arey [20] stated that the crystalline pigment granules of different animals have characteristic shapes. In man the inclusions of pigment are short; in birds the pigment assumes the shape of a needle. In my case the pigmented epithelial cells were suggestive of those in the retina of man and had a close resemblance to those in lower animals, such as birds. Olgie [21] and Campbell [22] reported the presence of pigmented epithelial cells in pineal tumors and thought they might represent a rudimentary retina.

16. Mallory, F. B.: Three Gliomata of Ependymal Origin, J. M. Research **3**:1, 1902.

17. Saxer, F.: Ependymepithel, Gliome und epitheliale Geschwülste des Centralnervensystems, Beitr. z. path. Anat. u. allg. Path. **32**:276, 1902.

18. Bielschowsky, M., and Unger, E.: Zur Kenntnis der primären Epithelgeschwülste der Adergeflechte des Gehirns, Arch. f. klin. Chir. **81**:61, 1906.

19. Uemura, S.: Zur normalen und pathologischen Anatomie der Glandula pinealis des Menschen und einiger Haustiere, Frankfurt. Ztschr. f. Path. **20**:381, 1917.

20. Arey, L. B.: Retina, Chorioid and Sclera, in Penfield, W.: Cytology and Cellular Pathology of the Nervous System, New York, Paul B. Hoeber, Inc., 1933, vol. 2, p. 743.

21. Olgie, E.: Tr. Path. Soc. London **50**:4, 1899.

22. Campbell: Tr. Path. Soc. London **50**:15, 1899.

The occurrence of cartilage in the pineal body is very rare, but it has been described in pineal tetratomas by Coats,[23] Weigert,[24] Falkson,[25] Horrax and Bailey [26] and recently by Bochner and Scarff.[27]

CASE 2.—*An astroblastoma of the pineal body in a man aged 45. Duration of symptoms, one month.*

History.—The patient had been well until two weeks before admission to the Cook County Hospital on March 21, 1933, when he began to suffer from diplopia and frontal headaches. The headache grew more and more severe, was constant, lasted throughout the day and was accompanied by vomiting.

Examination and Course.—The patient appeared well nourished. He lay very restlessly in bed, moving his hands about almost constantly. The temperature was 100.6 F.; the pulse rate was 64; the respiratory rate was 18 and the blood pressure was 134 systolic and 70 diastolic. Examination of the heart, lungs and abdomen revealed no pathologic changes.

The patient was unable to stand, and the gait was wobbly. There was slight past pointing with the right forefinger to the right. The pupils were slightly unequal and reacted sluggishly to light and in accommodation. There was paralysis of the right external rectus muscle with inability to look to the extreme right, and slight ptosis of the left upper eyelid was noted. The visual fields and the fundi were practically normal except for slight blurring of the margins of the disks. The tongue showed a slight tremor but did not deviate.

Reflexes: The biceps, triceps and radial reflexes were all sluggish. The right patellar reflex was absent, and the left was present. The reflexes of both achilles tendons were sluggish. The plantar responses were normal; the abdominal and cremasteric reflexes were also normal.

Laboratory Findings: The urine was normal. Roentgenograms of the skull revealed no pathologic changes. The white blood cell count was 14,600, of which 90 per cent were polymorphonuclears. The spinal fluid was under increased pressure and contained 48 mg. of sugar per hundred cubic centimeters. The Wassermann test was negative.

The symptoms grew steadily worse; the patient became semistuporous and delirous and died twelve days after he was admitted to the hospital. A diagnosis of meningo-encephalitis was considered, but a tumor of the brain was also strongly suggested.

Necropsy (Dr. R. H. Jaffé).—The following anatomic diagnosis was made: early stage of bronchopneumonia; subacute peptic ulcer of the duodenum; slight parenchymatous degeneration of the organs.

Macroscopic Examination: The brain weighed 1,455 Gm.; the consistency was soft; the dura was under tension and was smooth and shiny. The convolutions were slightly flattened. Between the leptomeninges over the posterior half of the convexity of each hemisphere were deep purple-red extravasations of blood. Similar

23. Coats, J.: Tr. Path. Soc. London **38**:44, 1887.

24. Weigert, C.: Zur Lehre von den Tumoren d. Hirnanhänge, Virchows Arch. f. path. Anat. **65**:212, 1875.

25. Falkson: Ein Chondrocystosarcom im dritten Ventrikel, Virchows Arch. f. path. Anat. **75**:550, 1879.

26. Horrax, G., and Bailey, P.: Tumors of the Pineal Body, Arch. Neurol. & Psychiat. **13**:423 (April) 1925.

27. Bochner, S. J., and Scarff, J. E.: Pineal Teratoma with Unusual Adamantinous Features, Am. J. Path. **10**:696 (Sept.) 1934.

extravasations were present about the superior aspect of the cerebellum. The vessels at the base were thin-walled. In the region of the pineal body was a mass, 15 by 10 by 16 mm., which was sharply circumscribed and consisted of a moderately firm, light pink-gray, finely granular tissue. The tumor was attached to the tela choroidea, the two internal cerebral veins crossing its upper aspect. The tumor separated but did not invade the optic thalami. At the base it extended into the lamina quardrigemina and broke into the sylvian aqueduct, which was filled with the same light gray and granular tumor tissue. The lateral ventricles were slightly dilated and filled with a blood-tinted fluid (fig. 7).

Fig. 7 (case 2).—Photograph of a tumor of the pineal body filling the sylvian aqueduct.

Microscopic Examination: The outer portion of the tumor was composed of loose, fibrillary connective tissue with many small and large dilated vascular sinuses. In one area a small remnant of tissue of the choroid plexus was seen invaginating the mass, and scattered about were laminated calcareous concretions. The stroma of the remaining portion was more compact and under low magnification showed numerous blood vessels, about which there was ample connective tissue. The thickened walls of the vessels often revealed a fine radial fibrillation and in places extended for a short distance between the adjacent cells (fig. 8). The endothelial cells of the vessels were swollen. Occasionally plasma cells were seen in the connective tissue. Between the vessels were many loosely scattered rounded or

irregularly angular cells with short, slender protoplasmic processes which formed a delicate and loose network. These cells tended to arrange themselves about the blood vessels. The nuclei were round and oval, containing a moderate amount of chromatin. Here and there were long processes emanating from the cell body and terminating on a nearby blood vessel or passing along the wall of the vessel for a short distance before becoming attached (fig. 9 *A* and *B*). Where the cells

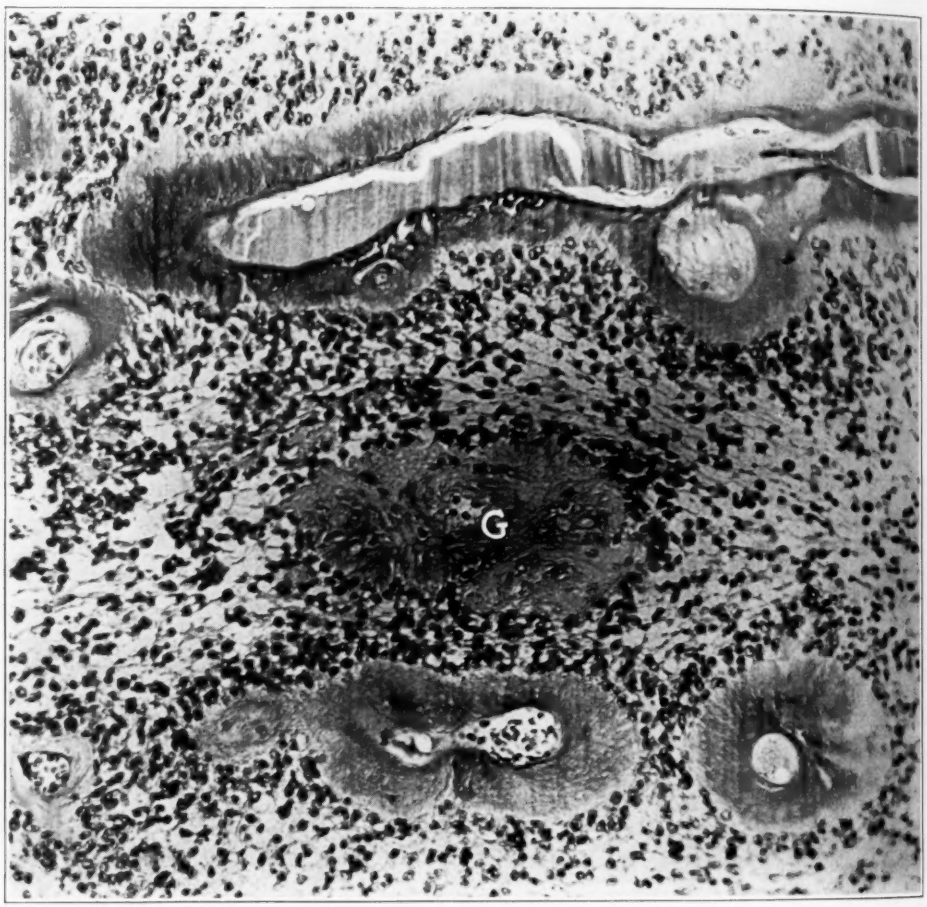

Fig. 8 (case 2).—A section of the tumor showing marked proliferation of the connective tissue about the walls of the blood vessel. *G* indicates a patch of fibrillary glia tissue. Mallory's phosphotungstic hematoxylin and eosin stain; × 150.

lay closer together the processes became indistinct. There were small patches composed of fibrillary glia (fig. 8 *G*). Occasional astrocytes and unipolar and bipolar spongioblasts were seen. Most of the cells and their processes showed marked regressive changes such as pyknotic nuclei and vacuolation of their cytoplasm. Elements of the normal pineal body were not definitely demonstrable in the tumor.

Summary of Microscopic Observations and Diagnosis.—The presence of an embryonic type of cells with a tendency to arrange themselves about blood vessels in a radiating fashion and to attach themselves to the wall of the vessel by long, thick processes terminating as vascular feet, with the presence of the characteristic feature of ample connective tissue about the blood vessels, gives this tumor a dis-

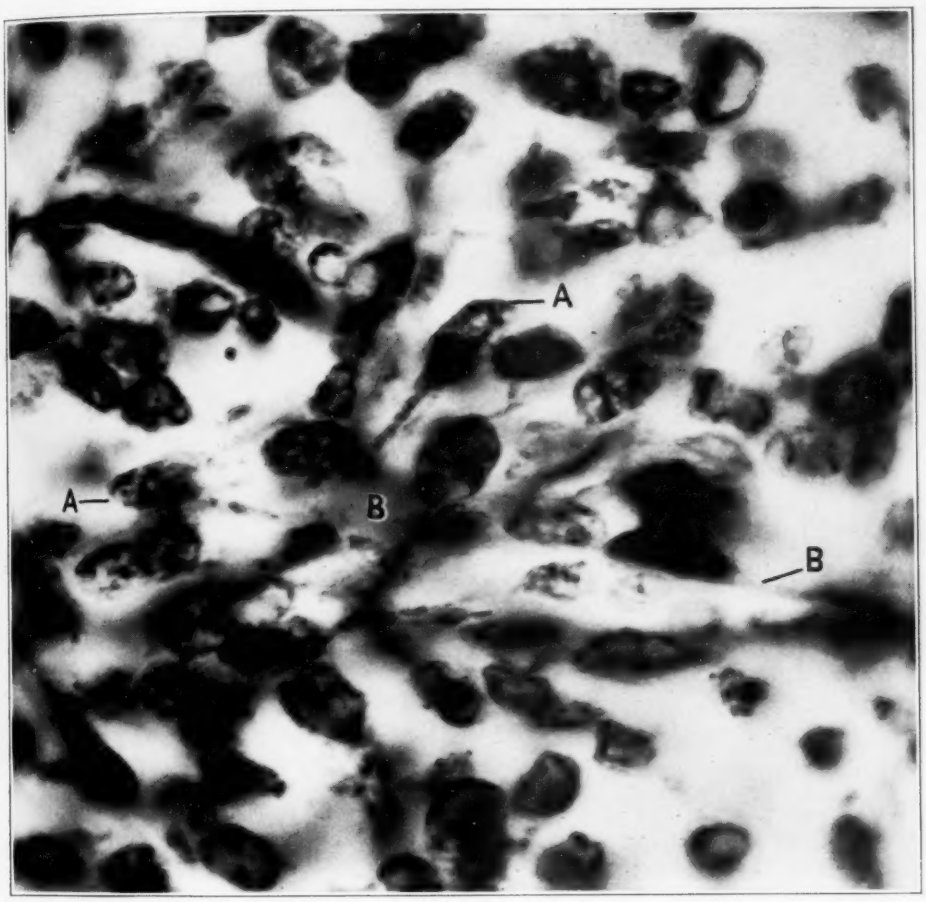

Fig. 9 (case 2).—*A* indicates a large process emanating from a glia cell and terminating on a nearby blood vessel (*B*). The vessel is not quite in focus. Fincher's modification of Hortega's silver-carbonate stain; × 1,200.

tinctive microscopic appearance which, according to Hortega,[28] Bailey and Bucy [29] and others, definitely establishes it as an astroblastoma.

28. del Rio Hortega, P.: Pineal Gland, in Penfield, W.: Cytology and Cellular Pathology of the Nervous System, New York, Paul B. Hoeber, Inc., 1933, vol. 2.

29. Bailey, P., and Bucy, P.: Astroblastomas of the Brain, Acta psychiat. et neurol. **5**:439, 1930.

Comment.—The histologic constituents of the parenchyma of the normal pineal body have been a matter of discussion, and apparently a definite conclusion has not been arrived at, in spite of the extensive work done by many investigators. Two or three types of cells are differentiated in the parenchyma of the pineal body, and accordingly the pineal body has been considered a lymphatic, nervous, neuroglial or glandular organ. As to the variety of cell elements described, the consensus today, according to Krabbe,[30] Hortega,[28] Horrax and Bailey [31] and others, is that the lobules of the pineal body are composed chiefly of specific parenchyma or pineal cells and neuroglia or interstitial cells. On the other hand, Tilney and Warren [32] and after them Globus and Silbert,[33] who in 1931 studied the evolutional stages of the human pineal body, failed to identify glial or neuronic elements and did not recognize spongioblastic or neuroblastic forms of pinealoma. Globus expressed the opinion that the cellular organization of the pineal body at an early stage of development pointed to a glandular character for at least the brief prenatal period. Bailey,[34] on the other hand, accepted the existence of ependymal canals which later disappear. The pineal cells, though closely related to nerve cells, are specific, as no one has been able to demonstrate in them the existence of axis-cylinders. Since the cells arise from the same epithelium as the nerve cells, some of them may become transformed into true ganglion cells, though it is a rare occurrence. Thus, according to Hortega,[28] Biondi and Pastori reported the presence of a typical ganglion cell in the pineal body, but he himself found only occasional "heterotopic elements."

Some types of tumor of the pineal body have been reported in the literature by Haldeman,[35] Dias [36] and others as glioma and by Businco [6] as neuroglioma, and recently a neuroblastoma and ganglioneuroma have been described from Cushing's clinic, while Horrax and Bailey [31] described in the pineal body the presence of glioblastic elements. The

30. Krabbe, K.: The Pineal Gland, Especially in Relation to the Problem of Its Supposed Significance in Sexual Development, Endocrinology **7**:379, 1923.

31. Horrax, G., and Bailey, P.: Pineal Pathology, Arch. Neurol. & Psychiat. **19**:394 (March) 1928.

32. Tilney, F., and Warren, L. F.: The Morphology and Evolutional Significance of the Pineal Body, (American Anatomical Memoirs, vol. 9, p. 7), Philadelphia, Wistar Institute of Anatomy and Biology, 1919.

33. Globus, J., and Silbert, S.: Pinealomas, Arch. Neurol. & Psychiat. **25**:1, (Jan.) 1931.

34. Bailey, P.: Intracranial Tumors, Springfield, Ill., Charles C. Thomas, Publisher, 1933, p. 331.

35. Haldeman, K.: Tumors of the Pineal Gland, Arch.Neurol. & Psychiat. **18**: 724 (Nov.) 1927.

36. Dias, A.: Pineal Tumors with Multiple Gliomata, Monatschr. f. Psychiat. u. Neurol. **76**:9, 1930.

presence in the pineal body of an astroblastoma, as described in this report, together with the aforementioned reports in which the neuroglial and nerve elements predominated, permits a conclusion that the pineal body is a neurogenic organ.

CASE 3.—*Calcified meningioma (psammoma) arising from the pia adjacent to the pineal body in a man aged 21, revealed by a roentgenogram.*

History.—A. W., a Mexican, was admitted to a surgical ward of the Cook County Hospital, where a diagnosis of tumor of the brain was made. The complaints at the time of admission were: weakness and spastic paralysis of the right side of the body for two and one-half years, difficulty in talking, vertigo and blurring of vision with diplopia for three months. A roentgenogram of the skull disclosed

Fig. 10 (case 3).—Roentgenogram of the skull revealing the calcified tumor in the region of the pineal body.

a calcified tumor in the midline of the cranial fossa above the tentorium in the region of the pons, posterior to the sella turcica. The tumor was thought to be an oligodendroglioma (fig. 10). A decompression was done. The intracranial pressure was normal, but a trocar met with resistance at a depth of about 3 cm. in the brain tissue. The resistance was overcome by slight pressure, and the ventricle was entered. The patient made an uneventful postoperative recovery, but his condition was not ameliorated. One week later (December 1932) he was admitted to the neurologic service with practically the same complaints except for the headache and vision, which were somewhat improved.

Examination and Course.—The patient was well developed; the temperature was 98 F., the pulse rate was 80 and the blood pressure was 100 systolic and 75 diastolic. There was a soft scar in the left temporoparietal region in the area of decompression. No rigidity of the neck was present. The pupils were dilated

and equal and did not react to light or in accommodation. There was loss of movements of the eyes above the horizontal level; other ocular movements were intact. The fundi as well as the visual fields were normal. There was bilateral muscular weakness of the lower part of the face, and movements of the lower jaw were restricted. The tongue showed a slight tremor and did not deviate on protrusion. Speech was slow and dysarthric, and there was some difficulty in swallowing.

There were right hemiparesis, with the tendon reflexes on the right more active than those on the left, bilateral ankle clonus and a bilateral Babinski sign. The finger-to-nose and heel-to-heel tests on the right showed slight ataxia. There was absence of the pharyngeal reflex; the jaw reflex was exaggerated. Sense of touch, pain and temperature was intact throughout.

The patient's headache did not subside, and he became drowsy. The area of decompression began to bulge. While eating one day he suddenly evidenced difficulty in breathing, became cyanotic and died.

Necropsy (Dr. R. H. Jaffé).—The anatomic diagnosis was: parenchymatous degeneration and beginning atrophy of the heart; brown atrophy of the liver; anemia and cloudy swelling of the kidneys; passive congestion and edema of the lungs.

Macroscopic Examination: Marked digital impressions were present in the inner table of the skull, and in the left parietal bone was a round defect 5 cm. in diameter which led into the left middle cerebral fossa. The defect was filled by adherent dura mater. In the skin of this region was a linear scar covered by hair. The brain weighed 1,640 Gm. The convolutions were flattened; the leptomeninges were thin, transparent and slightly injected; the basilar vessels were thin-walled. The left temporal lobe was loosely adherent to the dura in the region of the defect. The corpus callosum was flattened, and underneath this structure one could feel a lobular stony mass. It measured 50 by 40 by 40 mm. and was underneath the posterior half of the corpus callosum, where it occupied the posterior two thirds of the third ventricle. The ventricle was greatly dilated. The corpus callosum was pushed upward and was very thin. The tuber cinereum was dilated and rounded, and its walls were thinned. The optic thalami were displaced laterally and were much compressed by the mass, which excavated their median aspect. The corpora quadrigemina were much compressed and flattened and stood upright to the base of the brain. The pons was pushed downward and posteriorly. There was no trace of the pineal body or of the posterior commissure of the third ventricle. The mass was located entirely inside the brain, apparently originating from the choroid plexus near the pineal body. It was firm and had the consistency of stone, and even sawing was accomplished with great difficulty. The surfaces facing the ventricles were smooth. The color was light yellow-gray, quite uniform, with pale gray, ill defined foci. The lateral ventricles were greatly dilated.

Microscopic Observations: The tumor consisted of dense, coarsely trabecular connective tissue in which were embedded numerous calcium concretions. The connective tissue contained a few deeply stained, flat nuclei and very few blood vessels and stained from orange-red to bright red with the method of Van Gieson. The calcified part of the tumor appeared in the form of spherical, concentric bodies and irregular masses which resulted from a diffuse impregnation of the collagenous ground substance with lime salts. The spherical concretions often fused with the calcified substance, and irregular, fantastic structures resulted which looked like the trunks of dead trees. Here and there could be seen a small island of cellular tissue in the midst of the sclerosed and calcified tissue. These islands were composed of flat, fusiform cells with spindle-shaped nuclei and of spherical concretions which were smaller than those in the sclerosed parts. The concretions were derived

from hyaline bodies which had a great affinity for fuchsin and in turn could be traced to the fusiform cells. At first the cells formed themselves into concentric clusters and fused together; the nuclei disappeared, and in the hyalinized cell bodies lime salts became deposited first in the central parts. Some of the bodies revealed a calcified center with a hyalin-like ring about it and flat cells on the outside (fig. 11).

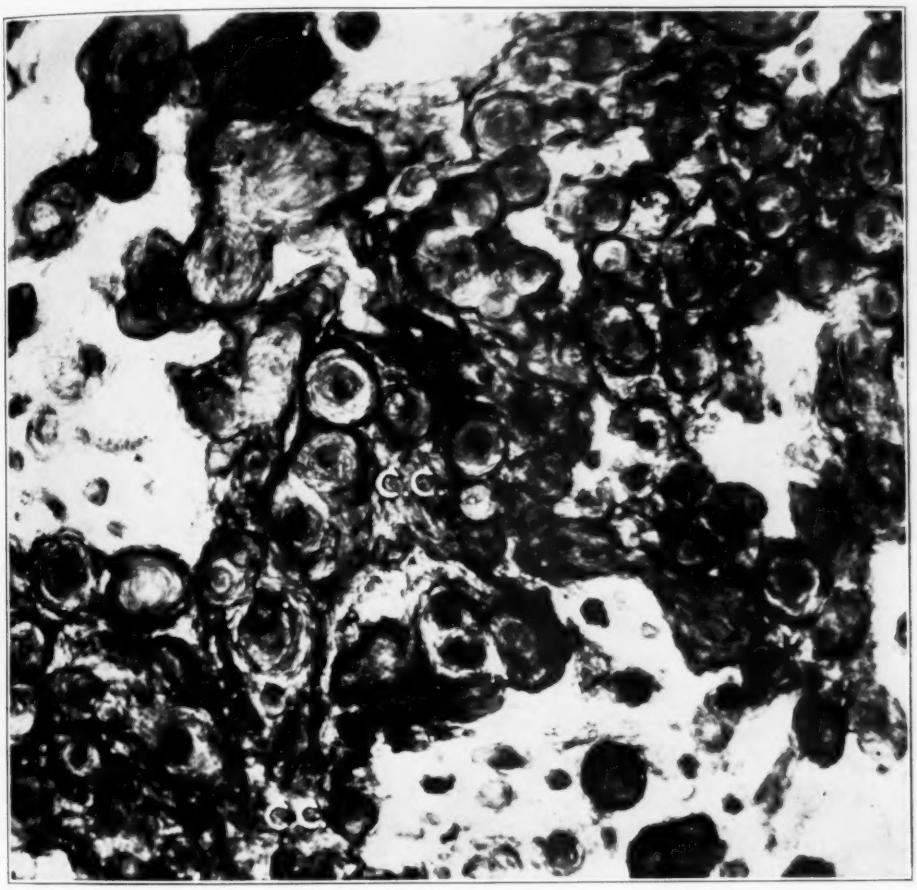

Fig. 11 (case 3).—A section of the tumor (psammoma) showing hyaline and calcareous spherical concretions with islands of cellular tissue (*C.C.*). Van Gieson's stain; × 150.

Comment.—From the histologic observations presented it is evident that the tumor was a calcified meningioma (psammoma) arising from the pia about the pineal body, which it had invaded and evidently destroyed, for no vestiges of this organ could be demonstrated. Meningioma is usually parasagittal, and its presence in the midline is rare

(Elsberg [37]). From the shadow cast on the roentgenogram, as in this case, a calcified meningioma must be considered as well as a possible teratoma of the pineal body, which frequently contains calcareous deposits, as in the case reported by Fassbender,[38] that of a girl, aged 7½, with pubertas praecox, in which from the roentgen findings a probable diagnosis of teratoma of the pineal body was made.

SYMPTOMATOLOGY OF TUMORS OF THE PINEAL BODY

Because tumors of the pineal body give a fairly characteristic symptomatology yet are so infrequently diagnosed prior to necropsy, a consideration of the symptoms produced by such tumors seems to be justified in a pathologic report of this nature.

The anatomic relation of the pineal body to the posterior part of the roof of the third ventricle, the splenium of the corpus callosum, the anterior quadrigeminal plate and the sylvian aqueduct produces a fairly characteristic syndrome for this area. Early in its development the tumor presses on the sylvian aqueduct and produces symptoms and signs of obstructive hydrocephalus and of intracranial hypertension, such as persistent headache, vomiting and vertigo. The localizing symptoms result from pressure on the quadrigeminal plate, affecting the nuclei of some ocular muscles and the tracts in the corpora quadrigemina. The most frequent and characteristic ocular signs, as pointed out by Horrax and Bailey,[26] Wilson,[39] Haldeman [35] and others, are the loss of conjugate movement upward of the eyes above the horizontal level and dilated pupils with loss of the pupillary light reflex. Diplopia, impairment of vision, paralysis of the abducens nerve and ptosis are other common associated signs. Pressure on the medial geniculate bodies usually causes disorders of hearing, as here lie the relay stations for the conduction of impulses from the cochlea to the cerebral cortex. Symptoms on the part of the neighboring structures, the cerebellum and pyramidal fibers, for instance, consist of nystagmus, ataxia and bilateral spasticity of the lower extremities. Involvement of the hypothalamic regions by pressure may be manifested by polyuria, adiposity (Marburg [40]), exophthalmos and tachycardia, but the symptoms on the part of the neighboring structures are usually indicative of the later stages of the illness. In the past, great clinical significance was

37. Elsberg, C. A.: Parasagittal Meningeal Fibroblastomas, Bull. Neurol. Inst. New York **1**:389, 1931.

38. Fassbender, F.: Ueber einen Fall von Praecositas somo-psycho-genitalis bei einem 7-½ Jahre alten Mädchen, Ztschr. f. Kinderh. **54**:642, 1933.

39. Wilson, K.: Case of Mesencephalic Tumor with Double Argyll Robertson Pupil, J. Neurol. & Psychopath. **3**:140, 1922.

40. Marburg, O.: Die Klinik der Zirbeldrüsenerkrankungen, Ergebn. d. inn. Med. u. Kinderh. **10**:146, 1913.

attached to the occasional presence of Pellizzi's syndrome—macrogenitosomia praecox, or precocious physical development in children, most marked in the genital system. This manifestation together with symptoms of tumor of the brain and localizing symptoms involving the quadrigeminal plate was considered suggestive of a tumor of the pineal body. Gutzeit,[41] in 1869, was the first to call attention to the relation of tumors of the pineal body to the sexual sphere. Since then authors from time to time have explained the relationship between teratoma of the pineal body and the occurrence of pubertas praecox, until 1920, when Askanazy [42] demonstrated that all such tumors were teratomatous. This conclusion has since been refuted, particularly by Horrax and Bailey and by others who have reported cases of pubertas praecox with tumor of the pineal body composed largely of undifferentiated pineal cells. Likewise, to disprove the relationship between tumor of the pineal body and pubertas praecox Horrax and Bailey,[26] Bailey [34] and Wieland [43] reported cases of tumor of the third ventricle and of the falx cerebri in which the pineal bodies were not involved but in which pubertas praecox was present. It is also known that pubertas praecox may occur with tumor of the adrenal glands (Krabbe [36]) or testes. The question thus is far from settled. In most cases of pubertas praecox studied the investigations have been limited to a study of the brain. More valuable information may be uncovered in the future by a study of the relation of pubertas praecox to the body as a whole.

As the onset of symptoms in the three cases reported here was beyond the age of puberty, evidence of pubertas praecox could not be expected.

CONCLUSIONS

Three cases of tumor arising in the region of the pineal body are reported with clinical and pathologic studies.

One was a mixed tumor composed of neuro-epithelial tissue, papillomatous choroid plexus, pigmented epithelial cells and cartilage; another was an astroblastoma. It is evident that both these tumors arose within the pineal body. The third tumor, a calcified meningioma, invaded the pineal body from the adjacent pia.

Pathologic studies of tumors of the pineal body seem to support the view that this organ is of neurogenic origin.

41. Gutzeit: Ein Teratom der Zirbeldrüse, Dissert., Königsberg, E. Erlatis, 1896.

42. Askanazy, A.: Die Zirbel und ihre Tumoren in ihrem funktionellen Einfluss, Frankfurt. Ztschr. f. Path. **24**:58, 1920.

43. Wieland, E.: Macrogenitosomia Praecox in a Four Year Old Boy with Cancer of the Third Ventricle and Intact Pineal Glands, Praxis (no. 2) **17**:1; 3 (Jan. 10) 1928.

DISCUSSION

DR. PERCIVAL BAILEY: In Dr. Zeitlin's first case the growth was obviously a teratoid tumor. Neuro-epithelium is obvious, and although it is not common in tumors of the pineal body it is often found in teratomas elsewhere in the body. It is difficult to judge from lantern-slides, but I wonder whether the papillary structures might not be interpreted as respiratory epithelium.

In the second case the tumor might well be an astroblastoma. One should remember, however, that the cells of the pineal parenchyma have also processes which end in the neighborhood of the blood vessels; so I should not like to accept the diagnosis of astroblastoma without more careful examination of the actual preparations.

In the third case, of course, the growth was not a tumor of the pineal body but arose doubtless from the meningeal tissue in the neighborhood of the pineal body. I have operated on patients with such a tumor.

The syndrome which Dr. Zeitlin has outlined seems clear when one reads about it in a book, but when one attempts to diagnose a tumor of the pineal body on the basis of this syndrome one often goes astray. All these symptoms can be and are produced by tumors in the neighborhood which do not arise from the pineal body, and it is very important for the surgeon to know exactly what may be the origin and position of the tumor in determining his mode of attack; unfortunately, it is difficult to reach a definite conclusion in these cases. I have had the experience of checking all these symptoms, having them carefully checked by others, making a ventriculogram and an encephalogram and nevertheless being finally wrong in my diagnosis.

DR. VICTOR E. GONDA: The second case seems to me to be the one I reported before this society on Feb. 18, 1932, and which has been reported in the transactions of the society (ARCH. NEUROL. & PSYCHIAT. **28**:950 [Oct.] 1932). I should like to know whether this was the same case.

DR. RICHARD H. JAFFÉ: I wish to say regarding the third case that Dr. Bailey was sent a section and he wrote me that there was no doubt that the growth was a meningioma.

DR. G. B. HASSIN: Microscopically, the tumor in the third case was certainly a meningioma.

DR. HOWARD ZEITLIN: Although the papillomatous epithelial structures might suggest a resemblance to respiratory epithelium, a diagnosis of papillomatous tissue of the choroid plexus could definitely be made in the first case. The presence of outpouching villi with their central core composed of connective tissue and small blood vessels, together with numerous granules in the cytoplasm of the epithelial cells resembling mitochondria, are all characteristic of papillomatous tissue of the choroid plexus.

Microscopically, normal cells of the pineal body could not be identified in the second case. The structures present were definitely those of an embryonic type of glia cell; they were interpreted as astroblasts.

The second case is the one mentioned by Dr. Gonda.

PSYCHOGENIC LOSS OF PERSONAL IDENTITY

AMNESIA

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In psychopathology every state of forgetting is called amnesia. We are interested here merely in cases of amnesia in which the subjects forget their own identity. To one's own identity belongs the connection with a specific social structure. One has relatives, friends, a place where one works and another where one lives. But the name and address are symbols of one's identity. In every-day life one identifies people by these criteria and they identify themselves in this way. A person's knowledge, insight and faculties are much less important in this respect. We speak about amnesia in this paper only when the consciousness is not deeply clouded, orientation is retained, and the possibility of forming impressions is not completely lost. However, when knowledge and general information have been impaired, in addition to the loss of identity and address, the case is still classified as amnesia.

Although this state is well known, special studies have rarely been devoted to it. At the ninetieth annual meeting of the American Psychiatric Association, Leavitt [1] discussed the problem. Newspapers often report such cases. During the World War amnesia as a defense reaction was frequently observed. Price and Terhune [2] and Henderson [3] reported such cases and were particularly concerned with the differentiation from malingering. Amnesia in relation to crime has also been carefully studied by Hapwood and Snell.[4] In not many cases have thorough studies been made and the subjects psychoanalyzed. Hamill [5]

From the Psychiatric Division, Bellevue Hospital.

1. Leavitt, F. H.: The Etiology of Temporary Amnesia, Am. J. Psychiat. **91**:1079, 1935.

2. Price, G. E., and Terhune, W. B.: Feigned Amnesia as a Defense Reaction, J. A. M. A. **72**: 565 (Feb. 22) 1919.

3. Henderson, D. K.: Amnesia as a Defense Reaction for Desertion, Rev. Neurol. & Psychiat. **16**: 151, 1918.

4. Hapwood, J. S., and Snell, H. K.: Amnesia in Relation to Crime, J. Ment. Sc. **79**: 27, 1933.

5. Hamill, R.: Amnesia and Pathologic Stealing, Arch. Neurol. & Psychiat. **12**:125 (July) 1924.

reported a case of pathologic stealing associated with amnesia, and Gordon [6] a case of dual personality with amnesia, in both of which psychoanalysis was carried out. In both cases there was intense parental repression followed by rebellion in the form of amnesia. Ribot [7] was more interested in the spectacular cases of double personality. In the books of Janet [8] one finds also a few remarks about this specific type. Though psychoanalysis has drawn new attention to the subject, the compilation by Fenichel [9] does not touch on it. E. Braun [10] in the newest German handbook gave merely a short description of the picture. Wechsler [11] reported two interesting cases of amnesia, one lasting a year and a half. Brown [12] mentioned amnesia briefly in one case in his book.

Amnesia is a well recognized pattern which plays a part in the community. We have therefore undertaken to study the problem based on the rich material of the psychiatric division of the Bellevue Hospital. It is well to begin by presenting a typical case.

Case 1.—N. C., a woman aged 38, approached a policeman in the street and said that she could not remember her name. She was admitted to the hospital. She said "I don't know anything about myself." She was depressed and agitated. The time of admission was about 2 a. m. After sleeping through the night she was interviewed by a physician, about eight hours after admission to the hospital, when she had spontaneously recovered. She gave the history that she had been twice married. The first marriage was unsuccessful because of the husband's sterility (mumps). She had married again ten years before admission, but had not had sexual relations with her husband in the past five years. She had been faithful to him nevertheless until eight months before admission to the hospital when she went to Florida, where she fell deeply in love with another man. She would like to have stayed in Florida. She also would have liked a divorce but did not want to disrupt her social life. She enjoyed sexual relations and missed them. She had arrived in New York two weeks before the episode of amnesia. The night of the attack she felt hungry and cold and went to get

6. Gordon, A.: Dual Personality Apropos a Case of Amnesia with Analysis, Arch. Neurol. & Psychiat. **16**: 379 (Sept.) 1926.

7. Ribot, T.: Diseases of Memory, New York, D. Appleton & Company, 1882; The Diseases of the Personality, Chicago, Open Court Publishing Company, 1881.

8. Janet, P.: L'automatisme psychologique, ed. 7, Paris, Félix Alcan, 1913, p. 493.

9. Fenichel, O.: Hysterien und Zwangsneurosen, Vienna, Internationaler Psych. analyt. Verlag, 1931.

10. Braun, E.: Psychogene Reaktionen, in Bumke: Handbuch der Geisteskrankheiten, Berlin, Julius Springer, 1928, vol. 5, pt. 1, p. 112.

11. Wechsler, I. S.: The Neuroses, Philadelphia, W. B. Saunders Company, 1929, p. 200.

12. Brown, W.: Psychology and Psychotherapy, ed. 3, Baltimore, William Wood & Company, 1934, p. 197.

something to eat. In the street she accidentally collided with a man and was shaken up. From then on she remembered nothing until she recalled her memory in the hospital.

The psychogenesis in the case is clear. From the warm climate of Florida where she found love, she came to a colder climate. She felt "hungry and cold" before the attack. She wanted to be warm and with the man she loved in Florida. There were other distinct relations to her early history which are of no interest here.

During the past three or four years, 63 cases of psychogenic amnesia have been collected and studied in the Bellevue psychiatric service. Twenty-two patients were admitted from January to June 1934, when the total number of patients admitted was 8,298, this number thus being 0.26 per cent of all new patients.

SEX AND AGE

Thirty-one patients were male and thirty-two were female. The oldest patient was 56 and the youngest 14, though another patient had a history of a previous amnesic episode at the age of 12. According to decades, there were none in the first, 13 in the second, 21 in the third, 17 in the fourth, 8 in the fifth and 4 in the sixth. There is definite preponderance in the earlier decades, 80 per cent of all patients being in the second, third or fourth.

PREVIOUS HISTORY AND PERSONALITY

In our series 15 patients had had one or more previous amnesic episodes. In addition, 6 had a history of dizzy spells and fainting attacks. Three had made suicidal attempts at some time in the past. One had a history of somnambulism. Another patient had a history of antecedent manic-depressive psychosis. Cases 2 and 3 are reported in more detail because of the significant earlier history.

Case 2.—I. P., a man aged 37, was admitted on Dec. 10, 1933, saying: "I don't know my name. I don't know where I live or whether I'm married." He recovered spontaneously after two days. He recalled that he had been attacked by several men immediately preceding the loss of memory. Interesting and probably significant was the history of being attacked by several men at the age of 3, when he was extremely frightened.

Case 3.—N. Q., a woman aged 54, who was admitted on Dec. 5, 1932, had approached a policeman because she could not remember anything about herself. Her memory was restored in less than a day with the aid of hypnosis. The history was that five years before she had been in an automobile accident in which she was injured, with resulting right hemiplegia and aphasia. She recovered from this except for some slight residual effects. On the day of loss of memory she looked out of the window and saw her daughter get into an automobile. She said "I was so nervous. I was afraid she was lost."

In both these cases a previous distressing and unpleasant memory was recalled just before the onset of the amnesia. Even more interesting were the circumstances in case 4.

CASE 4.—I. C., a woman aged 29, who was admitted on July 27, 1933, was very depressed and in a state of amnesia. Though her mind was deeply clouded and she did not recognize her mother or father, she was fairly well oriented about impersonal things. She was found in the subway, and had apparently fallen down the stairs. The amnesia continued for six days when she recovered with the aid of hypnosis. She then gave the history that eight years before, the father of her illegitimate child died. Since then she had had periodic amnesic episodes. These had usually followed a period of depression, once following the death of a sister. Six years before the present admission, she fainted in the subway and fell off the platform in front of a train, her right arm being cut off. It is of interest that the present attack also accompanied a fall in the subway. At the time she was on the way to visit a brother (who may be a substitute for her father).

Here again an unpleasant memory was recalled.

ETIOLOGY

In a number of instances there was either psychic or physical trauma immediately preceding the amnesic episode and precipitating it. For instance, in case 1 the last thing the patient remembered was unexpectedly colliding with some one in the street. Episodes in some of the other patients were instituted by quarrels. In one, the fright of an assault by several men was followed by the loss of memory (case 2). In two instances the patient was startled by an approaching automobile. In still another case a woman was alarmed by a Negro who accosted her. Case 5 is a good example of fright as a precipitating factor.

CASE 5.—N. M., a girl aged 14, was brought to the hospital by her father because several days before she had lost her memory and the next day was found on a park bench unable to tell where she had been. Although she had already recovered he brought her in for observation. The patient told of a quarrel with her aunt the night before, in consequence of which her mother slapped her. She had had a similar amnesic episode ten months previously which lasted for two days and was accompanied by mutism. This attack followed a fright from an encounter with two rats, one of which she accidently stepped on; she said "One of them jumped for my throat."

All these, however, were mere stimuli, for on going deeper into the background of the patient more significant conditions and conflicts were usually uncovered. By far the majority had some familial difficulty or an imminent economic problem. An interesting example of the former is furnished by case 6.

CASE 6.—G. B., a woman aged 30, was admitted on March 22, 1934, while depressed and unable to identify herself. The next day, with some persuasion, memory partially returned and from then on she gradually recalled more and more information about herself, though she still retained some blank periods

even on discharge. The story was that several years before she had run away from home because of a domineering father. She said that every time she made plans and prepared to go home for a visit there would develop some partial or complete loss of memory. For instance, while packing her clothes preparatory to the trip she would forget what she was doing. She was afraid to go home for fear she would have one of these attacks.

In addition, the desire to flee from some unpleasant marital situation frequently led to loss of memory. For example, one of our patients, who was the wife of a man with chronic alcoholism with whom she had had many difficulties, lost her memory and found herself wandering on Broadway. Another woman, whose husband expected perverted sexual relations, fled into amnesia. There were four unusual cases in which there was latent or conscious homosexuality, the amnesia being a result of some conflict arising from the sexual psychopathy. Case 7 is an excellent example of the condition in this group.

Case 7.—M. K., a woman aged 24, was found in the street unable to remember her name or where she lived. She was depressed and anxious and showed some twitchings of the muscles, especially of the left leg. Three days later, under superficial hypnosis, she revealed her name and address. She lived in a suburb of New York with a woman much older than herself for whom she apparently had a very deep unconscious homosexual attachment. She said she never cared very much about men. Earlier in life she had been very devoted to an aunt who, she said, "got along in the world without being married." She said she had not wanted to live after this aunt died five years before. She dreamed about her frequently. On the day of the amnesia she quarreled with the woman with whom she lived because she gave a gift to another friend. She felt very unhappy about it and came to New York, and the amnesia developed.

As a variation, a male homosexual patient of the overt type in a fit of jealousy over a "boy-friend" experienced a short period of amnesia.

In another important case, because of feelings of guilt arising from a conscious hate of the mother the patient had an episode of excitement in which she called for her father.

Case 8.—N. McK., a colored girl aged 15, was transferred to Bellevue Hospital from Seaview Hospital, where she had been hospitalized for pulmonary tuberculosis. While there she began to act peculiarly; she was at first restless and noisy and then became mute and uncooperative. On admission she continued to be uncooperative and would not answer questions. She frequently called "Daddy." After a week of this behavior she recovered and became cooperative. She denied any recollection of the entire episode. In the antecedent history it was found that she had a very strong attachment for the father from whom she had been separated by her mother. In consequence she did not feel a proper regard for her mother. Then ideas of guilt arose out of the realization of her unnatural feeling for the mother.

This patient was on the borderline of amnesia, in the wider sense, and loss of personal identity in which we are interested.

Economic difficulties were of the usual order, including financial reverses, unemployment and impending poverty, with all the resulting anxieties and fears. The condition in case 9 was unusual in this respect.

CASE 9.—S. R., a man aged 36, entered the hospital in a dazed, bewildered state, very depressed. He had been found overcome by gas, apparently in a suicidal attempt. He continued in this perplexed state, unable to grasp the situation or to remember what had happened. He frequently gave contradictory answers, sometimes remembering things he had just said he had forgotten. He gradually improved, however. Significant in the history was that the day before the suicidal attempt he had been promised a more responsible position with his salary increased.

This was an interesting reaction to a sudden increase in responsibility, probably with feelings of inadequacy. Of note in this case, also, was the intense subjective feeling of impairment of judgment and memory by the patient and his concern over it.

Case 10 is described because a partial analysis was possible and revealed important facts in the early history.

CASE 10.—A. O., a woman aged 36, was found in the subway unable to identify herself. On admission she was extremely agitated and depressed. She continued to be so, and all she could remember was "Johnny" and "Rue Galilée." Several hours after admission she was identified by a man; she did not recognize him at first but then recalled everything. This man was "Johnny." The patient was married to a man twenty years older than she. She was dissatisfied and felt superior to her husband. For the past three months she had been participating in a clandestine affair with Johnny. A week before the illness she had had an argument with her husband and left him to stay with Johnny. On the day of the amnesia they had agreed that she should go back to her family. The idea was very disagreeable, and as she went down the subway suicidal ideas entered her mind. Instead amnesia developed. She recovered eight hours later in the hospital.

A short analysis revealed that the mother had always been very strict. The father died when the patient was 3 and her only conception of him was that he had a beard. "All men with beards are disgusting," she said. She had definite desires of self-expression; she wanted to be an actress and to write. Because of these ideas she came in conflict with her mother. She envied her older sisters who were artists, lived in Paris (Rue Galilée) and never married. She said she was the "ugly duckling in the family." She entered a convent school at an early age, where restrictions continued. The mother wanted her to teach. The idea was repulsive, and to escape it she married at the age of 17. She did not love the man she married, who was much older than she. He probably became a substitute for the father. She even exaggerated the actual difference between their ages. He also was strict, did not care much for social activities and disapproved of any excessive activities on her part. During the early part of married life the patient frequently walked in her sleep. She would leave her sleeping husband and go on somnambulistic jaunts, occasionally walking out of the house. During the twenty years of married life she made abortive attempts at self-expression, but for the most part she led a life of intense repression. Her early resentment toward her parents was transferred to the husband who was a father substitute. The amnesia was a rebellion and protest against authority.

DURATION

The duration was anywhere from a few hours (the shortest period that could be estimated was about three hours) to about a month, as in case 11.

CASE 11.—F. H., a man aged 34, was found on the street complaining of sudden inability to see and was admitted to the ophthalmologic service of Bellevue Hospital on April 17, 1934. Complete examination of the eyes revealed no pathologic change. The patient refused to eat or to give any information and was transferred to the psychiatric division. The blindness disappeared on the second day after admission. He professed complete amnesia for his whole previous life and could not identify himself. His attitude was rather silly and indifferent. He continued to be amnesic in spite of hypnosis, with and without the aid of hypnotics. The amnesia was anterograde; he forgot things that happened during his stay in the hospital. For instance, he declared that he had never seen the examiner on the day after he saw him. The amnesia reached a ridiculous point at one phase, so that a Ganser syndrome was seriously considered. He even denied recognizing his own face in the mirror and professed other impossible losses of memory. In spite of this, psychometric examination showed that the patient was of at least average intelligence. His manner continued unconcerned and silly, and he made little effort to recall his memory. On May 11, about twenty-five days after the onset, without being asked, he volunteered the information that this was the day on which he had landed in this country thirteen years before, saying that the date in the newspaper reminded him. He gave his true name and details of his past life. He stated that he had had financial difficulties in the past year.

In case 11 it is remarkable that practically nothing of importance was discovered about the psychic etiology. It may be mentioned here that the longer the duration the more one has the impression that a secondary mechanism is playing a part. In many of the spectacular cases of dual personality the actual cooperation of the physician plays a part in prolonging the amnesia. Notable among such cases are those mentioned by Azam,[13] Goodhart and Sidis[14] and Prince.[15]

In another case the patient had fugues lasting one, two and three months during which he was partially amnesic. However, there was an organic background, so that this case cannot be included among those of purely psychogenic amnesia. This case will be reported in more detail later (case 24). In several other instances the patient wandered about for several days or a week before asking for help. Sometimes during these extended attacks the patient wanders far from home. Case 12 is a good illustration of this type.

13. Azam: Hypnotisme, double conscience et altération de la personnalité, Paris, B. Baillière et fils, 1887.

14. Goodhart, S. P., and Sidis, B.: Multiple Personality, New York, D. Appleton & Company, 1905.

15. Prince, W. F.: The Doris Case of Multiple Personality, Proc. Am. Soc. Psychiat. Research **9**:1, 1915; **10**:701, 1916.

CASE 12.—J. Q., a man aged 34, was referred to the Clinic for Mental Hygiene for examination. The history was that on Aug. 30, 1933, he received his pay check in New York, bought a glass of beer and was on his way home from work. The next thing he remembered was when he found himself in Indiana on the bank of a river, feeling weak and with a "chalky taste" in his mouth. After wandering around for a while he returned home. He could not account for the episode or remember how he got there. Memory for the four days was totally gone. No obvious reason for the fugue was elicited. He went away with his pay check. When memory returned, he had spent it, which is a common occurrence in amnesia.

Statistically, in 27 cases the amnesia lasted less than twenty-four hours; in 21 cases the amnesia lasted from one to five days; in 7 it lasted about a week; in 2, about two weeks, and in 2, three weeks or more. In 2 cases the duration was indefinite because the patient had recovered by the time of admission, but the attack probably endured less than a week.

KNOWLEDGE DURING AMNESIA

Many patients recover quickly before the degree of amnesia during the attack can be estimated; in these cases it can at best only be surmised. The main symptom is the loss of identity; the patient does not know his name or address. He approaches some one in the street, most often a policeman, and complains that he cannot remember his name. One of our patients was unusual because she knew her name but not her address. Frequently the patient can give some approximate information and isolated details about himself, which is of little or no use in identifying him or locating relatives. Not infrequently he hints at the cause of the absence of memory; he may mention money or some conflict of opinion. One case was unique in that the loss of memory was not so much in the foreground as was the inability of the patient to remember the circumstances of his life, i. e., whether he was married and details about his business. Sometimes the memory is spotty, so that it reminds one of a Ganser syndrome. In most cases the condition is not amnesia in the sense of loss of personal identity but amnesia in the sense of loss of memory of the past.

Case 13 is of interest because during the amnesia the patient denied recognizing his own face in the mirror.

CASE 13.—J. F., a married Jew aged 50, was admitted on Feb. 9, 1934, complaining of complete loss of memory and identity. He was supposed to have left a town in Pennsylvania and arrived in New York a week before, but did not remember anything that had happened before. His memory for events of the past week in New York was hazy. He had some recollection of going to see "a lot of shows." His knowledge of general current information was almost nil. He declared that his mind was a complete blank. When his sister and a niece visited him the next day he did not recognize them. He even said that he could not talk Jewish, which he evidently knew. He denied understanding the most

basic conceptions of every-day life. When asked if he recognized his face in the mirror, he said "My face looked strange—it did not look natural." On the fourth day in the hospital the patient recovered partly with the aid of hypnosis. The history was that he believed himself a "mental healer." He would hypnotize people and believed that he helped them. Several months before the illness a girl he was treating in order to try to make her leave a bad life accused him of having sexual relations with her. He was arrested, and it cost him $500. On the day of the onset of the amnesia he had been near the Union Station, had seen an advertisement for an excursion to New York and took it.

General information about current events and about every-day familiar knowledge and experience was frequently poor, as demonstrated by the routine informal memory test of the psychiatric examination. Some of the patients professed no knowledge at all; their minds were a complete blank. Some could not do even ordinary calculations. Others retained an adequate fund of general information. Case 14 is paradoxical.

CASE 14.—A. G., a man aged 40, who was admitted on Nov. 19, 1932, had gone to the home of a minister and asked for help; he could not remember his name. He was brought to Bellevue Hospital. He remained amnesic until November 26, when the sound of a piano playing in the wards helped to restore his memory. He had been completely amnesic. However, during the period of amnesia the Well's memory test revealed a memory span well above normal.

Though his past was a blank, actual formal testing of the efficiency of memory indicated good function. In some cases in which the name of the patient was known and presented to him, it was not recognized. Similarly, patients occasionally would not recognize close relatives.[16] Nevertheless, the inability to recall was usually retrograde and did not include events that transpired following the onset of the amnesia. In contrast was the condition in case 11.

Quantitative memory retention tests were not given to many patients during the amnesia, but from the general behavior and replies to routine questions it appeared that the ability to retain new information was often not obviously impaired. In 5 cases standard intelligence tests were given during the amnesic period, and in each instance the patient made at least an average grade in spite of the loss of recall. The psychogalvanic reaction was investigated in a number of cases. However, the problem is still being studied and will be reported when more conclusive results are obtained.[17] In 3 instances, because of mutism and unresponsiveness the extent of the patient's knowledge could not be determined.

16. Often the relatives treat the patient as a malingerer and doubt the genuineness of the amnesia.

17. Wechsler, David: Personal communication to the authors.

BEHAVIOR DURING AMNESIA

The onset of amnesia usually occurs when a change in some long-standing disagreeable situation becomes imminent. There is a preceding period of depression. The patient most often finds himself wandering in the street or in some public place, as in a hotel or a railroad station. Sometimes the patient wanders around for days before seeking help. It is of interest that none of our patients have had sexual relations during the amnesia. Frequently the actual behavior during this period remains rather vague. Then, with dismay, the patient realizes that he has forgotten his identity and becomes alarmed. The most frequent course of action is to go to the first policeman with the problem. On admission to the hospital the most common mood is one of depression and perplexity. The patient is agitated and apprehensive, and often cries. Occasionally he is terrified, mute and unresponsive. Most patients make an apparent effort to recollect the past. Rarely, they are calm. One adolescent girl attempted to dramatize the situation.

CASE 15.—B. S., a girl aged 15, was admitted to the hospital on Jan. 5, 1933. She was rather calm and stated that she did not know anything about herself. On her person was a hand-printed note which read as follows: "Sun Tan Soy: This girl is in a state. Take her and do your worst. Be careful for the dicks. Found her wandering near Mott. She doesn't know her name, where she came from. In return let me have Solie. Be careful. I am sending her to you. (Signed) Wah Tong." In addition, she had a Chinese ring and a book in which was written the following: "Tong war: Three packages—opium given to Ming Tan Soy—Hatchet Keeper."

When questioned about these things the patient said she had found them in her hand. When various relatives appeared she did not recognize them until the seventh day of the amnesia. She recovered completely. She said that she had been amusing herself writing stories which concerned Chinese characters. She had never had any direct dealing with Chinese.

The depressive features in our cases generally continued during the absence of memory, though it frequently became less severe, and when the amnesia disappeared the patient's mood became normal. In one case, however, the recollection of the unpleasant incident which led to the amnesia made the patient irritable and depressed for several days following recovery. As has been stated, in rare cases the mood was calm, cheerful or even hypomanic. In most of these instances simulation had to be considered.

COMPLICATIONS AND ATYPICAL CASES

In a large percentage of the cases the condition was uncomplicated, being straightforward amnesia. Alcoholism was a factor in only a few cases and then it was incidental to the general depression and had no appreciable effect on the clinical picture. There was one case, however, in which alcohol played an important part.

CASE 16.—J. K., a man aged 28, who was admitted to the hospital on June 14, 1934, had acute alcoholism and was mute and very depressed. Several hours later he began to talk but could not tell his name or address. He said that his father had died a month before and he had been drinking since. He soon recovered completely from the amnesia but professed amnesia for the mute episode.

In 2 cases the condition was complicated by hysterical amaurosis; one of these has been cited already. In case 17 the blindness dominated the picture.

CASE 17.—L. M., a colored woman aged 24, was found in the hallway of her mother's home saying she was blind and going to die. She was brought to the Bellevue Hospital and continued to be depressed, complaining of blindness, though she made movements that obviously indicated that she was not amaurotic. Twelve hours later, after sleeping through the night, she woke and said she could see. The story was that she had been at a party, and had had a drink of whisky. Some one there said something about her brother being killed (he had been killed about a year before). Following this she remembered nothing until she found herself in her mother's home and was "blind."

As already mentioned, hysterical fainting, headaches, noises in the ears and other somatic complaints may be involved in the clinical picture.

The following case is an interesting variation in what is otherwise a classic case of amnesia.

CASE 18.—M. B., a girl aged 20, left a difficult home situation in Florida, and went to a neighboring city. There she lost the memory of her identity for about a day. After recovering, she hitch-hiked to a point near New York. She took a train into New York and on arriving at the Grand Central Station again became amnesic. She was taken to the Bellevue Psychiatric Hospital, where, with the aid of hypnosis, she recalled everything.

This condition was similar to a fugue except that the amnesia punctuated rather than involved the entire flight.

RECOVERY FROM AMNESIA

Of the total number, 47 patients recovered spontaneously. A number of them recovered automatically on the appearance of a relative, though some gave no indication or made no effort to recognize relatives. One patient reacted by becoming extremely agitated and running away from the relative. On the other hand, many recalled their identity spontaneously without external aid. Often in the middle of the night or on awakening in the morning the patient would announce his identity to the nurse.

In 25 cases hypnosis was attempted. In some it was tried after the patient had recovered but with a residual blank space for the occurrences during the time of the amnesia. In 3 this period was partly recalled, and in 1 it was completely recalled with the aid of hypnosis. Of the

25 cases in which hypnosis was attempted, in 8 the efforts were wholly successful, and in 6 partly so. The patient ordinarily recovered during or immediately after the procedure. Sometimes the hypnosis was merely an aid in completing the recovery from amnesia which had partially disappeared spontaneously. One of the most remarkable cases in which hypnosis was used successfully was case 19.

CASE 19.—B. H., a man aged 26, was admitted on Jan. 6, 1933, totally amnesic for his whole previous life, though his general fund of information of current events was intact. He continued to be amnesic until January 10 when, with the aid of paraldehyde, he was hypnotized. During hypnosis he revealed many identifying details and in a disconnected fashion the events preceding the amnesia. He told of a fight with a friend over a watch. Hypnosis was then discontinued, and memory was completely restored except for the hypnotic period and the events of the amnesia. He asked where he was and who the examiner was. His story was that on the night of January 4 he had had a fight with a friend whom he was choking when two other men knocked him down. Following this he got up and had a few drinks. The next thing he remembered was sitting on a bed in the hospital with two doctors questioning him (posthypnosis).

In another case, suggestion by pressure on the eyeballs was used effectively to produce recovery. In still another patient, who was involved in a lawsuit the threat to expose the patient to the police produced a speedy recovery. Here the question of malingering was brought up. In a number of cases the patient was given a pencil and was told to allow his hand to write automatically. In 3 cases significant information was obtained in this manner. In some cases the name was recalled piecemeal, letter by letter, with the persuasion of the physician. In 2 cases, association with dream material was contributory in the cure of the patient.

CASE 20.—A. W., a man aged 28, entered the hospital in an amnesic state which continued for five days. The past history, which was obtained later, was that he was the son of an English sea-captain who had been stationed with the fleet at Hongkong. The patient had been trained in the English navy. Ten years before he had had an accident; he fell 65 feet (19.5 meters), which incapacitated him for further service. On admission to the hospital he said that he had been frightened by a taxicab. Hypnosis was attempted on the fourth day and he reenacted the traumatic scene. He said, "I am falling, I am falling." The next day he was hypnotized again and had two dreams. In the first, he was sailing on the Japanese Sea and saw two sharks swallowing meat. From this he remembered Shakespeare, which he kept repeating and became very excited. On the second hypnosis, he said "We were going down the river Avon to the funeral of Caesar and that's how I got to Mark Antony." Then he associated sharks, Shakespeare, Brutus, Antony. He said "What general won Lochinvar—Clive—Clive. That's my father's name. My name is Anthony Wallace."

It is of interest that the memory of 2 patients was restored by hearing the playing of a piano in the ward. Another patient regained his memory when he hallucinated his mother's voice calling to him.

In the majority of the cases, when memory returned it did so completely and at once. However, a good many patients recuperated gradually during several days. Some have even been discharged from the hospital with fragments of the past still missing. Frequently there is a permanent blank period, which is apparently never recalled after recovery. This is the period lasting from the onset of the amnesia to the time when the patient decides to confide his difficulty to some one else. This blank sequence is occasionally recalled with the help of hypnosis, but more frequently it is not.

DIFFERENTIAL DIAGNOSIS

This is not always simple, and often the diagnosis is not absolutely certain until after the patient has recovered. Practically the entire range of psychiatric classification must be considered in differential diagnosis. Schizophrenia, manic-depressive psychosis, organic disease of the brain, including trauma to the head, cerebral arteriosclerosis, presenile dementia, aphasia, carbon monoxide encephalopathy and Korsakoff psychosis and simulation were some of the possibilities to be eliminated. It is best to demonstrate these contingencies with cases.

CASE 21.—J. G., a man aged 40, walked into a police station on Oct. 23, 1932, and stated that he did not know his name or anything about himself. He was very untidy, with a beard and swollen feet. He appeared to be somewhat depressed, although he said he was happy. Under hypnosis, four days later, he could not tell his name but was able to tell a few facts of his life. He thought his trouble had started seven weeks before, and told a number of other things. The next day he refused to remember these things. On November 14, more than three weeks after admission, he remembered everything. He said, "I couldn't get my name out of me—I was frightened. I had an idea I wouldn't use my name any more. I got too frightened to tell it." He told of organized persecutory trends which he had had; he felt that the Masons were after him at one time. According to his relatives he was very seclusive. He had been put in a sanatorium about seven years before, had disappeared and had not been heard from since.

In this case the diagnosis was schizophrenia. In case 22 a diagnosis of manic-depressive psychosis was made.

CASE 22.—C. H., a man aged 59, when admitted to the hospital on Jan. 16, 1934, was extremely depressed, apprehensive and bewildered. He complained of pain in the back and said that he did not know who he was or where he came from. He stayed in the hospital for over two weeks, during which he continued to be profoundly depressed and made numerous hypochondriac complaints. After a few days, with persuasion and suggestion he spelled out his name and gradually recalled many of the facts of his previous life. However, his depression continued to be so severe that he was transferred to Manhattan State Hospital for longer institutionalization. No cause for the amnesia or depression was ascertained.

It is interesting that in the anamnesis in our psychogenic cases injuries of the head and carbon monoxide poisoning producing amnesia

were not rare. This shows how difficult it is even in cases of organic involvement to exclude psychogenic factors. In case 23, in which amnesia followed injury of the head, the etiology was subsequently discovered on a merely psychogenic basis.

CASE 23.—C. P., a man aged 35, was admitted on May 14, 1934, with marked discoloration and swelling of the right eye and with the history that he had been hit over the head and robbed. He said, "I can't tell my name or anything." He could not remember being hit and did not know anything about his past life. He did not know whether he was married. Two days later he recalled his name, and the amnesia completely disappeared except for the traumatic incident. The spinal fluid and roentgenograms of the skull were normal. The Wells memory test on May 21 showed a memory quotient of 82 per cent. He was discharged with a diagnosis of organic amnesia caused by trauma of the head. About three weeks later he was readmitted to the hospital, again amnesic, without any evidence of trauma. He presented a clearcut case of hysterical amnesia. He had sufficient familial and financial difficulties to account for it.

The usual picture in trauma to the head is a loss of memory for the traumatic event, especially if it is accompanied by confusion or unconsciousness.

In case 24 there was definite organic disease of the brain. The patient had fugues which were at least partly psychogenic.

CASE 24.—A. R., a man aged 50, who was brought to the Bellevue Hospital for observation, three or four years before, had financial reverses and lost most of his money. With this there was a change in personality. Whereas formerly he had many friends and was a good mixer, he lost all friends and became morose and irritable. Familial disagreements began, and he would disappear from home for two or three days at a time. He would explain that he had been away on business but never told where. Then he began to have longer fugues; the first time he disappeared in February 1933 with a few dollars in his pocket. In May he was found in a neighborhood that was familiar to him, dirty and neglected. He was very depressed and cried. He could not tell where he had been or how he lived. He came home and was happy for a while, but in August he disappeared again and was found in October in circumstances similar to those of the previous attack. This was again repeated from November 1933 until February 1934, when he was admitted to the Bellevue Hospital for examination. At the beginning of his stay in the hospital he was depressed and somewhat dull. However, he gradually became more amiable and cheerful. He told little about what had happened during the fugues. Psychometric examination revealed disturbances of a generalized sort, especially in retention and perceptual tests. The score with the Wells memory test was 55 per cent. Physically, except for some slight peripheral sclerosis of the vessels, he showed nothing abnormal. Encephalography revealed a small amount of air in the lateral ventricles and a considerable amount of air in the subarachnoid space, probably indicative of cortical atrophy. He was discharged from the hospital with the diagnosis of cerebral arteriosclerosis, with fugues probably of psychogenic origin.

Amnesia for the events occurring during and following a convulsive seizure is well known. Case 25 is an unusual example.

CASE 25.—J. A., a man aged 36, was committed to the Psychiatric Division of Bellevue Hospital from the City Magistrate's Court for observation. He had been found wandering around suspiciously in a cellar and was charged with unlawful entry. When found he said he was looking for his brother, who he said lived only two blocks from there. The address which he gave as his brother's, however, was in another city. When he was brought to court he claimed that he did not remember how he got in the cellar or what he was doing. On transfer to the hospital he maintained this story; he had no recollection of the events which transpired in the cellar. A Ganser syndrome and even schizophrenia were considered, but the diagnosis remained in doubt for over two weeks when the patient made it himself by having a major convulsive seizure in the hospital.

The usual picture in such cases is for the patient to be found in a dazed condition after a convulsive seizure. When admitted to the hospital, without any previous history and at the same time unable to identify himself because of the postepileptic confusion a diagnosis of psychogenic amnesia is occasionally made. The correct diagnosis is recognized only after the patient recovers from the confusion and gives the history of previous epileptic seizures.

Case 26 is an unusual example of both simulation and hysteria playing a part.

CASE 26.—A. O., a girl aged 19, on Nov. 30, 1930, approached a policeman on the street and said she could not remember anything. She was brought to the Bellevue Hospital and remained amnesic for more than two months. She was given every freedom about the hospital. Hypnosis was attempted. At first the patient was a poor subject; she would go into a deep sleep and would not make any contact. She gave a fictitious name at first. During this time she showed very unstable behavior emotionally. About two and a half months after admission another amnesic patient entered the hospital and the first patient watched her respond quickly to hypnosis. After that she gave significant information during hypnosis. She could not talk when hypnotized so that she made all her responses with hand gestures. In this way she gave her father's and sister's names. After the hypnosis her father's name was presented to her and she became wildly excited and even hallucinated her father. Finally, her relatives were brought and identified her. Before she left, the patient admitted that she had had no amnesia whatsoever and that she knew all about herself from the first. She said she went to a policeman because she "wanted to get away from it all," and thought she would be sent to a state hospital where she would starve herself to death (she had refused to eat in our wards). She refused to be hypnotized when she first came in because she was afraid she would give herself away. During her stay she often wondered why her people did not come to the hospital to look for her. As a matter of fact they had been there and asked for her by name, but she had given a fictitious one. She finally submitted to hypnosis because she was afraid we would think she was "fooling" but always asked for sleeping medicine in order to go to sleep and not talk.

Cases 27 and 28 are examples of evident simulation.

CASE 27.—F. R., a girl aged 20, who was admitted to the hospital on Feb. 28, 1933, had approached an officer and told him she could not remember her

name or address. The day after admission she was recognized by one of the hospital employees as a former patient. At first she denied her identity, but she soon admitted that she simulated the amnesia to get away from her husband. Investigation revealed that although she was only 20 she had a long history of asocial behavior, including many sexual misdemeanors and a superficial suicidal attempt and had been in various reform institutions from which she had run away. Wherever she had been she was found to have been unreliable in all her statements and even fantastic in some of her confabulations.

CASE 28.—E. H., a woman aged 24, was admitted to the hospital on June 6, 1934, complaining of inability to remember her name and address. She stated that the last thing she remembered was being startled by a loud noise. She was calm and not depressed. In the wards she was agreeable and happy, even singing and entertaining the other patients. She continued amnesic until the next day when her sister identified her and she was discharged. On being released she stated that she knew her name all the time, and had used simulation as a means of escape from her family, who had oppressed her.

This study does not deal with amnesia in criminal cases, but one can see in the preceding cases how fluctuating the borderline between true amnesia and simulated amnesia can be. However, we hope that our description of cases of patients without criminal background will help in the differentiation between simulated and nonsimulated cases.

COMMENT

Although none of our patients was observed long enough to allow deep psychoanalysis, the material allows some conclusions concerning the psychologic structure involved. In 1 case in which the amnesia occurred after the death of a lover, the amnesia led to an accident in which the patient lost an arm (run over by a subway train). In another case the patient contemplated suicide by throwing herself in front of a subway train, but she resisted and amnesia developed. In these and other cases one has the impression that the amnesia is self-punishment arising from a feeling of guilt; it is a partial suicide. The psychogenic blindness in 2 cases preceding the amnesia probably had a similar meaning.

In many cases one finds a deep disappointment in the love object. It is a going away from the love object. One is dead for the love object. One removes oneself (suicide), but one removes the others at the same time. The tendency to punish them is often obvious.

Economic problems are often given as the cause of amnesia. One should be skeptical about such a possibility. One finds easily that there are usually deeper motives. A man had to sell a valuable picture and became amnesic, but he needed the money for the defense of his mother, who was accused of murder.

Amnesia is often a giving in to a stronger force. One of our patients became amnesic after being robbed of money he needed for the

family. It is seemingly a simple way out. In another case the patient became amnesic when pushed by a car, but in this case a deep love conflict was in the background.

It is remarkable that, as far as our information goes, in no case had sexual experiences taken place during the amnesic period.

One deals with a well known pattern which can be easily used. Comparatively superficial conflicts are sufficient. Since the pattern is publicly well known, it is comparatively often used for direct simulation.

In some cases there is an organic nucleus. Amnesia of the organic type, after an attempt at suicide by gas or by accident, may furnish an easy pattern for later use.

On the whole, amnesia is a weak attempt of a weak personality to escape conflicts which are chiefly conflicts of actual life, but of course these conflicts have relation to the more infantile reaction types, especially to the Oedipus complex. It is the fear of being punished by the family, by the father and mother or their representatives, which leads to an escape which does not harm the person too much.

THERAPY

In the interest of the patient and his family the amnesia should be removed as quickly as possible. When urgent questioning does not help, automatic writing or hypnosis should be used. But the psychotherapeutic task is not finished when the amnesia has disappeared. One should try to secure insight into the problems of the patient and to find the deeper motives which have led him to attempt to escape from reality and from his identity.

SUMMARY

Sixty-three cases of psychogenic amnesia are reported; 31 patients were male and 32 were female; 80 per cent of all the patients were in the second, third or fourth decade.

Fainting attacks and suicidal attempts were important in the previous history.

Some unpleasant social conflict, either financial or familial, was significant in the immediate cause of the amnesia. There were four cases in which homosexuality played a part.

The duration varied from three hours to several months. Twenty-seven patients, or almost half, recovered in twenty-four hours; 21, in from one to five days; 7, in about a week; 2, in about two weeks, and 2, in three weeks or more.

Cases of so-called amnesia are characterized by the loss of personal identity. In addition, general knowledge, information and memory for past events is mostly poor. The ability to retain new information during

the amnesia was often, but not regularly, preserved. Patients were usually puzzled and perplexed.

Forty-seven patients recovered spontaneously. In 25 cases hypnosis was attempted, and in 14 of these it was partly or wholly successful. Other methods, such as persuasion, automatic writing and association with dream material, aided in recovery.

In differential diagnosis schizophrenia, manic-depressive psychosis, organic disease of the brain, trauma of the head, cerebral arteriosclerosis, presenile dementia, aphasia, carbon monoxide encephalopathy, Korsakoff psychosis, epilepsy and simulation had to be considered.

Psychologically, behind the superficial conflicts which precipitated the amnesia deeper motives are found. The conflicts of actual life are related to the more infantile reaction types, especially the Oedipus complex. It is an attempt to escape from punishment and at the same time self-punishment by effacing one's own personality (psychologic suicide).

The amnesia as such should be removed by persuasion, suggestion and hypnosis. When the patient has recovered from the amnesia one should try to help him to obtain a deeper understanding of the emotional conflicts.

TUMORS OF THE FRONTAL LOBE

AN ANATOMIC AND PATHOLOGIC STUDY

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This study is the result of an analysis of the anatomic site of and the histopathologic observations on a series of 314 tumors of the frontal lobes. One of us (Adson [1]) has recently commented on the operability of brain tumors and the problems arising from lesions in the anterior cranial fossa.

This series includes all histologically verified neoplasms of the frontal lobes encountered at the Mayo Clinic up to Jan. 1, 1933. No metastatic lesions have been included in the series, and no tumors have been certified on the basis of the presence of cystic fluid alone.

The value of a consideration of a series of histologically verified and classified tumors of the brain is obvious, from the standpoint of both the surgeon and the pathologist. It must be pointed out, as Learmonth and Voris [2] have stated, that such a series does not give the actual incidence of each type of tumor because of the exclusion of many cases in which a tumor was probably or almost certainly present, such as the cases in which cystic fluid alone was obtained. Probably most of these so-called uncertified tumors would fall into the glioma group. However, such a series does illustrate the relative frequency of each type of growth in instances in which specimens come to the pathologist either for biopsy or for necropsy.

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This material was taken in part from a thesis submitted by Dr. Voris in partial fulfilment of the requirements for the degree of Master of Science in Neurosurgery at the University of Minnesota.

1. Adson, A. W.: Operability of Brain Tumors, Ann. Surg. **100**:241 (Aug.) 1934.

2. Learmonth, J. R., and Voris, H. C.: Points in the Surgery of the Frontal Lobes of the Brain, Arch. Surg. **27**:506 (Sept.) 1933.

ANATOMIC CONSIDERATIONS

We have included in this study all neoplasms that were wholly or partially situated in or pressing on the frontal lobes, as they are ordinarily defined anatomically, or on the corpus callosum. Anatomically speaking the frontal lobe includes that part of each cerebral hemisphere which lies anterior to the fissure of Rolando, superior to the fissure of Sylvius and external to the island of Reil. On the inferior surface it is bounded posteriorly by the olfactory stria and by the stem of the sylvian fissure (this last being concealed by the overhanging tip of the temporal lobe), and on the mesial surface it is bounded inferiorly by the sulcus cinguli. On its external surface it includes the following gyri from behind forward; the motor, premotor and superior, middle and inferior frontal gyri. On its inferior surface it takes in the orbital gyri and the gyrus rectus, and on its mesial surface, the mesial continuation of the gyrus rectus and the superior frontal gyrus (marginal gyrus), including the anterior two thirds or three fourths of the paracentral lobule. For a more detailed description of the gyri and sulci of the frontal lobe the reader is referred to the standard anatomic descriptions, such as those by Ranson,[3] Tilney and Riley,[4] Hardesty[5] and Villiger.[6]

Certain parts of the rhinencephalon, namely, the olfactory bulb and tract, the lateral, medial and intermediate olfactory stria, the anterior perforated substance, the para-olfactory area (Broca's area), the subcallosal gyrus and the anterior two thirds of the gyrus cinguli, have such an intimate anatomic association with the frontal lobes and the corpus callosum that we have not attempted to differentiate them from these structures in this study. Further, so little is understood of the normal or pathologic physiology of the olfactory areas that any such attempt would be of little significance.

For a description of the blood supply to the frontal lobe the reader is referred to that given by Learmonth and Voris.[2] Baldy[7] has described in detail the rôle of the anterior cerebral artery in the blood supply of the frontal lobe.

The fiber tract connections of the frontal lobes have been described by many authors; Hardesty's, Ranson's, Tilney and Riley's and other

3. Ranson, S. W.: The Anatomy of the Nervous System from the Standpoint of Development and Function, Philadelphia, W. B. Saunders Company, 1923.

4. Tilney, Frederick, and Riley, H. A.: The Form and Functions of the Central Nervous System, ed. 2, New York, Paul B. Hoeber, Inc., 1923.

5. Hardesty, I.: The Nervous System, in Morris, Henry: Human Anatomy, ed. 8, Philadelphia, P. Blakiston's Son & Company, 1925, vol. 8, p. 787.

6. Villiger, E.: Brain and Spinal Cord, ed. 3, Philadelphia, J. B. Lippincott Company, 1925.

7. Baldy, R.: Les syndromes de l'artère cérébrale antérieure, Paris, 1927.

standard descriptions are readily available. Rosett [8] has recently presented evidence that the so-called occipitofrontal association tract, or subcallosal bundle, is in reality a bundle of corticospinal, corticothalamic and corticopontile fibers and that there is no direct occipitofrontal association path. The question of the long and short association fibers of the cerebrum requires further study.

The efferent pathways of the frontal lobe, the corticospinal, corticobulbar and corticorubral pathway from the motor area and the frontopontile pathway from the frontal cortex anterior to the motor and premotor areas are well known and need no emphasis. The afferent pathways have been less well known and less emphasized but are no less important. Poliak [9] studied these paths in primates and presented his work in a valuable monograph. According to his studies the thalamocortical fibers to the precentral area are almost as numerous as those to the postcentral area. As Clark [10] and Ranson and Ingram [11] stated, the thalamocortical radiation comes from the entire lateral thalamic nucleus. Poliak showed that it is transversely segmented in individual fans perpendicular to the long axis of the hemisphere. These run in both the anterior and the posterior limb of the internal capsule, the rostral half of the segments coming from the rostral segments of the thalamus and supplying the precentral and prefrontal (in front of the precentral) regions. The fans are also longitudinally segmented, so that the fibers from the dorsal portion of the thalamus reach the dorsal zones of the cortex, and those from the ventral portion reach the ventral zones of the cortex. The individual fans incline with their upper extremities oralward in front and occipitalward behind, so that they reach the frontal and the occipital pole, respectively. This thalamocortical radiation is entirely unilateral. In addition, Poliak found among the corticofugal fibers numerous fibers to the caudate nucleus and the globus pallidus. The existence of these connections in man has been denied by Lhermitte.[12]

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9. Poliak, Stephen: The Main Afferent Fiber Systems of the Cerebral Cortex in Primates; An Investigation of the Central Portions of the Somato-Sensory, Auditory, and Visual Paths of the Cerebral Cortex with Consideration of Their Normal and Pathological Function, Based on Experiments with Monkeys, University of California Publications on Anatomy, Palo Alto, Calif., University of California Press, 1932.

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11. Ranson, S. W., and Ingram, W. R.: The Diencephalic Course and Termination of the Medial Lemniscus and the Brachium Conjunctivum, J. Comp. Neurol. **56**:257 (Dec.) 1932.

12. Lhermitte, Jean: Le lobe frontal, Encéphale **24**:87 (Jan.) 1929.

When the fact is recalled that the medial lemniscus, carrying proprioceptive impulses from the trunk and extremities, terminates in the lateral thalamus, the importance of these thalamofrontal connections is apparent. Any explanation of the so-called "cerebellar phenomena" in cases of lesions of the frontal lobe must take these afferent connections into account as well as the frequently mentioned frontopontocerebellar pathways.

The portion of the cerebrum belonging to the frontal lobes includes several physiologically different areas. Histologically it has been divided by various investigators into a varying number of so-called fields, based on microscopic differences in the various cell layers of the cortex.

Hines,[13] in an excellent and complete review, summarized the literature on cerebral localization up to 1929. As she pointed out, the frontal lobe includes: such well defined and electrically excitable areas as the motor or precentral area (field 4 of Brodmann), which lies in the motor gyrus; the premotor, or intermediate, precentral area (field 6 of Brodmann), which lies in front of the precentral area; the posterior third of the inferior frontal convolution (field 44 of Brodmann), the motor speech area of Broca (usually situated on the left), and an area (field 46 of Brodmann) in the center of the second or middle frontal convolution which when electrically stimulated causes conjugate movements of the eyes to the opposite side. In addition, there is a large mass of so-called silent cortex which is more than equal in mass to the areas just mentioned and was subdivided by Brodmann into about fifteen additional fields on the basis of histologic differences in the stratification of the cells of the cortex.

A great deal of experimental work and investigation has been carried out with reference to the functions of these various areas. Bucy[14] has recently shown that the premotor cortex (field 6 of Brodmann) in monkeys is electrically excitable and that complex progressive and rhythmic movements can be obtained by stimulation of the premotor cortex in the absence of the motor cortex. The threshold of excitability is higher for the premotor cortex than for the motor. A different type of response is obtained when the premotor cortex is stimulated in the presence of the motor cortex than when the motor cortex has been removed. Fulton,[15] also working with primates, obtained similar results and also experimentally removed the premotor cortex. He included as the syndrome of the premotor area an impairment of skilled movements without gross loss of motor power, spasticity and increased tendon

13. Hines, M.: On Cerebral Localization, Physiol. Rev. **9**:462 (July) 1929.

14. Bucy, P. C.: Electrical Excitability and Cyto-Architecture of the Premotor Cortex in Monkeys, Arch. Neurol. & Psychiat. **30**:1205 (Dec.) 1933.

15. Fulton, J. F.: Forced Grasping and Groping in Relation to the Syndrome of the Premotor Area, Arch. Neurol. & Psychiat. **31**:221 (Feb.) 1934.

reflexes, forced grasping and vasomotor disturbances of all of the contralateral extremities. These observations seem to be in accord with Herrick's [16] concept that the premotor centers determine which excitable areas (motor cortex) will be activated and in what sequence. Thus the premotor cortex is placed above the motor cortex as another step in the "final common path" for all sorts of intentional control mediated by the cortex as a whole.

Many workers have carried out extensive experiments in ablation on the so-called silent areas of the frontal lobe, both in primates and in lower mammals (especially in the cat and dog), with the view of determining the normal physiologic function of this part of the frontal lobe. As Herrick [16] pointed out, this region is scarcely represented at all in lower mammals and nowhere does it approach the development seen in the brain of man. Hence, the attempts (Bianchi's,[17] for example) to carry the results of such experimentation over into interpretations of human physiology are not anatomically well founded, and the conflicting results of many workers bear this out. Franz,[18] for example, found no emotional changes or loss of instinct or of long-standing habits in cats after extirpation of the frontal lobes. There was a loss of recent sensorimotor associations (habits), but the ability to relearn these was retained even after bilateral frontal lobectomy.

German and his associates,[19] on the other hand, found no permanent disturbance in dogs after removing either frontal lobe, but on removing both lobes a loss of all but the most simple acquired habits, definite postural disturbances and obvious mental confusion with apparent inability to recognize persons or any but the simplest commands took place. Their animals were able to relearn the more simple sensorimotor habits, but not complicated ones. Jacobsen,[20] after injuring the frontal and prefrontal areas of monkeys, found a loss of complicated habits (parietal injury caused the same effect) with no impairment of learning ability or permanent emotional change.

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16. Herrick, C. J.: Brains of Rats and Men: A Survey of the Origin and Biological Significance of the Cerebral Cortex, Chicago, University of Chicago Press, 1926.

17. Bianchi, Leonardo: The Mechanism of the Brain and the Function of the Frontal Lobes, translated by J. H. Macdonald, Edinburgh, E. & S. Livingstone, 1922.

18. Franz, S. I.: On the Functions of the Cerebrum: I. The Frontal Lobes in Relation to the Production and Retention of Simple Sensory-Motor Habits, Am. J. Physiol. **8**:1 (Oct.) 1902.

19. German, W. C.; Harvey, S. C., and Claiborn, L. N.: An Experimental Study of the Function of the Frontal Lobes in Dogs, Arch. Neurol. & Psychiat. **27**:961 (Oct. 6) 1932.

20. Jacobsen, C. F.: A Study of Cerebral Function in Learning: The Frontal Lobes, J. Comp. Neurol. **52**:271 (April) 1931.

Bolton,[21] after careful pathologic study of the brains of insane persons more than thirty years ago, came to the conclusion that the prefrontal region (frontal and prefrontal areas) "was the region concerned with attention and general orderly coordination of psychic processes." Herrick [22] pointed out the intimate relation of the frontal cortex (frontal and prefrontal areas) with the thalamus through the anterior peduncle of the thalamus, a connection that has already been referred to. There are considerable clinical data (summarized by Tilney and Riley, as well as by Herrick [22]) to support the conclusion that the thalamus is the center for correlation of affective experience. With this in view, the thalamofrontal connection may provide for the addition of effective impulses of thalamic origin to the sensorimotor patterns of the frontal and prefrontal areas.

Certainly the evidence at hand is sufficient to necessitate a separate consideration of the cortex anterior to the premotor area and of the premotor and motor areas in any attempt to correlate clinical symptoms with the anatomic situation of neoplasms. It is ample, we believe, to warrant an additional separation of the "silent frontal cortex" into two fields: a frontal field proper and an extreme prefrontal field, the latter barely, if at all, represented in animals lower than man. The divisions suggested by Campbell [23] answer this purpose satisfactorily and have the advantage of being familiar to students in this field.

As it is intended to follow this paper with an analysis of the symptoms presented in the cases in which the tumors mentioned here occurred, it is obvious that it is necessary to subdivide the series, so far as possible, on the basis of the anatomic situation of the tumors with respect to the various regions of the frontal lobes. For this purpose, we have subdivided the frontal lobe into areas corresponding to those given by Tilney and Riley, who based their division on the work of Campbell.

These areas are, from front to back: the prefrontal, frontal, premotor (intermediate precentral) and motor (precentral). The prefrontal area includes: on the lateral and polar surfaces of the hemisphere, the cephalic (approximately a fourth) portion of the middle, superior and inferior frontal gyri; on the mesial surface, the portions of the marginal (superior frontal) and rectus gyri lying anterior and ventral to the genu of the corpus callosum, and on the orbital surface, all of the area lying mesial to the external or orbital sulcus and anterior to the transverse orbital sulcus. The frontal area on the lateral surface of the frontal lobe has its caudal boundary represented by an imaginary line lying from

21. Bolton, J. S.: The Functions of the Frontal Lobes, Brain **26**:215, 1903.

22. Herrick, C. J.: An Introduction to Neurology, ed. 3, Philadelphia, W. B. Saunders Company, 1922.

23. Campbell, quoted by Tilney and Riley.[4]

4.5 to 5 cm. in front of the fissure of Rolando. Its cephalic boundary is represented by a similar, irregularly curved line averaging about 2 cm. caudal to the frontal pole. On the mesial surface it includes the portion of the marginal (superior frontal) gyrus situated above the anterior half of the body of the corpus callosum and its genu. On the orbital surface it covers a small area lateral to the external orbital sulcus and posterior to the transverse orbital sulcus. The premotor (intermediate precentral) area lies posterior to the frontal area. Its posterior boundary is likewise indistinct but is approximately represented by a line generally parallel with and from 1.5 to 2 cm. in front of the fissure of Rolando. This is continued on the mesial surface of the hemisphere so that this area includes the posterior part (about a fourth) of the marginal (superior frontal) gyrus and the anterior half (approximately) of the paracentral lobule. The motor area lies posterior to the premotor area and extends to the depth of the fissure of Rolando, which is its posterior boundary. It extends mesially into the paracentral lobule over an area corresponding to its width on the lateral surface of the hemisphere.

CLASSIFICATION OF TUMORS ACCORDING TO SITUATION

In classifying the tumors of this series on the basis of areas in the frontal lobes which they involved it is obvious that in many cases of infiltrating neoplasm, although the surgeon is able to obtain a specimen for biopsy and thus pathologically to verify the tumor, exploration does not reveal the entire extent of the tumor; accordingly, we are not justified in placing the lesion in any but the broad and general anatomic divisions. However, in 153 instances in this series we do have dependable information from exploration or necropsy as to the anatomic extent of the tumor. This information is in all cases the result of gross observation by inspection and palpation or both. The fact that the extent of the tumors in cases of infiltrating glioma has not been checked microscopically is, of course, a source of error, as these tumors often infiltrate the brain beyond the areas of gross involvement. On the other hand, these same infiltrating gliomas, especially at their peripheries, may have within them nerve fibers and even ganglion cells which are still anatomically and, probably, physiologically, intact, and in part at least they may still be carrying out their ordinary functions. Clinically, there is evidence to confirm this, as many patients with infiltrating glioma do not present symptoms commensurate with the gross or microscopic extent of the neoplasm; so from a clinical standpoint the two factors just mentioned may to some extent offset each other. At any rate, we feel justified in presenting these data as a basis for a later correlation with a survey of symptoms in patients with these lesions.

Situation of Tumors According to the Side Involved.—Gibbs,[24] in reviewing 262 tumors of the frontal lobe from Cushing's clinic, found that 131 were on the right side and 109 on the left and 22 were bilateral. In the present series the tumor was on the right side in 112 instances (36 per cent) and on the left side in 127 (40 per cent), and was bilateral in 75 (24 per cent).

In this series, as in that of Sachs,[25] there were more lesions on the left side than on the right, although not in such great proportions, and there was a definitely larger portion of bilateral lesions than in any of the series of Gibbs, Sachs, Hare[26] or Pisani.[27] As will be seen, this is accounted for in part by at least two factors: (1) the large number of basofrontal endotheliomas, which are practically all bilateral, and (2) a total of 38 tumors that involved the corpus callosum, most of them extending across the median line. Two tumors confined entirely to the corpus callosum are included with the bilateral tumors. It may be added parenthetically that the series includes 33 basofrontal endotheliomas and 5 endotheliomas arising from the sphenoid ridge. A report of a case in which 1 of the endotheliomas of the sphenoid ridge occurred has been included in a recent paper on this subject by Voris and Adson.[28]

Situation of Tumors According to Lobes Involved.—One hundred and twenty-three tumors in the series (39 per cent) were entirely confined to the frontal lobes, 152 (48 per cent) originated in the frontal lobes but involved other lobes of the cerebrum, the corpus callosum, or the basal ganglia, and 38 (12 per cent) definitely involved some portion of the frontal lobe but had their origin in other portions of the brain. Two tumors confined to the corpus callosum are also included. In 1 instance there were 2 separate and distinct tumors, 1 a gangliocytoma in the prefrontal area and the other a spongioblastoma multiforme in the frontoparietal region of the same side; the tumors are counted as occurring separately.

The adjacent structures involved by the 152 tumors which originated in the frontal lobes were: parietal lobe in 68 instances, parietal and temporal lobes in 13, parietal lobe and basal ganglia in 6, parietal lobe

24. Gibbs, F. A.: Frequency with Which Tumors in Various Parts of the Brain Produce Certain Symptoms, Arch. Neurol. & Psychiat. **28**:969 (Nov.) 1932.

25. Sachs, Ernest: Lesions of the Frontal Lobe: A Review of Forty-Five Cases, Arch. Neurol. & Psychiat. **24**:735 (Oct.) 1930.

26. Hare, C. C.: The Frequency and Significance of Cerebellar Symptoms in Tumors of the Frontal Lobes, Bull. Neurol. Inst. New York **1**:532 (Nov.) 1931.

27. Pisani, D.: I tumori del lobo frontale, Riv. oto-neuro-oftal. **3**:289 (July) 1926.

28. Voris, H. C., and Adson, A. W.: Meningiomas of the Sphenoidal Ridge with Unilateral Exophthalmus: Report of Two Cases, S. Clin. North America **14**:663 (June) 1934.

and corpus callosum in 3, insula in 3, insula and temporal lobe in 7, insula and parietal lobe in 2, insula and basal ganglia in 6, corpus callosum in 5, corpus callosum and basal ganglia in 13, basal ganglia in 7, temporal lobe in 16 and hypothalamus in 3.

The preponderance of invasion of the parietal lobe is outstanding. The 16 tumors which involved the temporal lobe were all endotheliomas that pressed on the tip or the superior surface of the temporal lobe as well as on the frontal lobe. Infiltrating tumors of the brain can invade the temporal from the frontal lobe, or vice versa, only by first involving either the insula or the parietal lobe.

The origin of the 38 tumors which involved the frontal lobe was: parietal lobe in 9 instances, insula in 2, temporal lobe and insula in 3, corpus callosum in 15, septum pellucidum in 2, basal ganglia in 5 and hypothalamus in 2. In this group the corpus callosum predominates as the seat of origin, with the parietal lobe ranking next.

Anatomically Verified Tumors of the Frontal Lobes.—When these data were tabulated it was found that there were no lesions involving the premotor area alone and that in the two largest groups the tumors occurred in the frontoprefrontal areas (50) and in the entire frontal, prefrontofrontal and premotor-motor areas (30).

In the group of 153 tumors for which we had exact information as to their gross anatomic extent is included a subgroup of 49 neoplasms which were confined to the frontal lobe and did not grossly invade other parts of the cerebrum. The areas involved by these 49 tumors were: prefrontal in 7 instances, frontal in 7, premotor in none, motor in none, frontal-prefrontal in 19, premotor-frontal in 3, premotor-motor in 3, prefrontal-frontal-premotor in 6, frontal-premotor-motor in 1 and prefrontal-frontal and premotor-motor in 3.

It is from this group that our most enlightening correlation of gross anatomic extent of the tumor with the clinical findings in the case should come. More than half of the tumors in this subgroup (33, or 67 per cent) occurred in the frontal and prefrontal areas, either separately or together, that is, in the so-called silent area of the frontal lobe.

PATHOLOGIC CONSIDERATIONS

Microscopic sections from each of the 314 tumors in the series have been examined, and the tumors have been classified according to a classification based on those of Bailey and Cushing[29] and Penfield,[30]

29. Bailey, Percival, and Cushing, Harvey: A Classification of the Tumors of the Glioma Group on a Histogenetic Basis with a Correlated Study of Prognosis, Philadelphia, J. B. Lippincott Company, 1926.

30. Penfield, W. G.: Classification of Brain Tumors and Its Practical Application, Brit. M. J. **1**:337 (Feb. 28) 1931.

with slight modifications. There were 194 gliomas in the series, and they were classified as follows: medulloblastoma, 1; oligodendroblastoma, 19; spongioblastoma multiforme, 113; polar spongioblastoma, 5; astroblastoma, 6; ependymoma, 5; astrocytoma, 28; oligodendroglioma, 9; gangliocytoma, 5; mixed type, 1, and unclassified, 2. The remaining tumors were classified as follows: endothelioma, 109; hemangioblastoma, 6; sarcoma, 2; lymphosarcoma, 1; epidermoid cyst, 1, and chondroma, 1.

The percentage of gliomas (62) is considerably higher than Cushing's [31] figure of 42.5 among 2,023 certified intracranial tumors. The large number of pituitary tumors (17.8 per cent) and acoustic neuromas (8.7 per cent) in Cushing's series makes his total percentage of gliomas, which were practically all intracerebral or intracerebellar, comparatively smaller than in a series confined to tumors of one of the lobes of the cerebrum. Elsberg's [32] series of 767 intracranial tumors contains 59 per cent gliomas. Pisani's series of 240 tumors of the frontal lobe reported on in the literature contains only 26.5 per cent gliomas, but 13.3 per cent of the tumors in this series were classified as sarcoma, and probably many of these would fall into the glioma class when thoroughly studied. Hare's series of 50 tumors of the frontal lobe contains 52 per cent gliomas, and Sachs' series of 45, 40 per cent.

It is interesting to compare the incidence of spongioblastoma multiforme (36 per cent) and astrocytoma (9 per cent) in this series with that in other series. Cushing's figures (based on his entire series) were spongioblastoma multiforme, 10 per cent, and astrocytoma, 12 per cent; Elsberg's, 12 per cent and 8 per cent, and Hare's, 20 per cent and 22 per cent. The preponderance of spongioblastoma multiforme (now called glioblastoma multiforme by Cushing) in the series presented is probably due in part to the fact that we have based our criteria for classification of gliomas on the principle that malignancy of a tumor should be estimated from the appearance of the most malignant portions of that tumor. In other words, we have classified each tumor on the basis of its most malignant portion in spite of the fact that in some cases the larger portion of the neoplasm was relatively benign. For example, 90 per cent of a given tumor may have the typical appearance of an astrocytoma or astroblastoma, but if 10 per cent reveals giant cells, mitotic figures and endothelial proliferation of the walls of the blood vessels we should classify that tumor as spongioblastoma multiforme.

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31. Cushing, Harvey: Intracranial Tumors; Notes upon a Series of Two Thousand Verified Cases with Surgical-Mortality Percentages Pertaining Thereto, Springfield, Ill., Charles C. Thomas, Publisher, 1932.

32. Elsberg, C. A.: The Parasagittal Meningeal Fibroblastomas, Bull. Neurol. Inst. New York **1**:389 (Nov.) 1931.

One tumor in the series has been classified as an atypical medulloblastoma. It occurred in a child 5 years of age and was very extensive, involving both frontal and parietal lobes. It is of interest that 5 tumors in the series are classified as ependymoma; 1 of these was well differentiated and was a typical papilloma of the choroid plexus. The other 4 were more primitive; 3 of them contained typical oligodendroblasts, and mitotic figures were plentiful. Since the present tendency is toward simplification in the classification of gliomas, we have grouped all these tumors as ependymomas. There was 1 glioma which we have been unable to classify except as a mixed tumor and 2 others are listed as unclassified because insufficient tissue was obtained for biopsy.

The percentage of endotheliomas (35) in this series is high, Cushing's figure being 13.4 for his entire series, Elsberg's, 13.2, Pisani's, 7.9, Hare's, 40, and Sachs', 31. Our figure is higher than for any series except Hare's. As Frazier and Alpers [33] pointed out, three of the favorite sites of origin of this type of tumor are included in the regions adjacent to the frontal lobes, namely, the olfactory groove, the sphenoid ridge and the anterior half of the falx cerebri. Hence one should expect a high percentage of endotheliomas in any series of tumors of the frontal lobe.

Six tumors (2 per cent of the series) are classified as hemangioblastomas. The occurrence of these tumors above the tentorium has been questioned in the past, although Cushing and Bailey [34] in their monograph on the subject accepted 4 reported on in the literature as being probably of this type and in a footnote they referred to 3 tumors possibly of this type in their own series. It is of interest in this connection that 3.2 per cent of Pisani's series were classified as angiosarcomas, and this group probably contains, in part at least, tumors similar to those that we have classfied as hemangioblastomas. Like the tumors to which Cushing and Bailey referred, our tumors all grossly resembled meningiomas and 3 were grossly attached to the dura, although all had on microscopic examination the structure of a hemangioblastoma.

There were 2 true sarcomas of the brain. These were rapidly growing tumors and possessed an architectural arrangement definitely related to the blood vessels. Leaving out of account the possibility of sarcoma developing from the leptomeninges, which has been dis-

33. Frazier, C. H., and Alpers, B. J.: Meningeal Fibroblastomas of the Cerebrum; Clinicopathologic Analysis of Seventy-Five Cases, Arch. Neurol. & Psychiat. **29**:935 (May) 1933.

34. Cushing, Harvey, and Bailey, Percival: Tumors Arising from the Blood Vessels of the Brain; Angiomatous Malformations and Hemangioblastomas, Springfield, Ill., Charles C. Thomas, Publisher, 1928.

cussed by Bailey,[35] the presence of the cerebral vascular tree certainly affords ample opportunity for the origin of sarcoma.

One tumor classified as lymphosarcoma may or may not have been primary in the brain. In the case in which this tumor occurred cerebral symptoms were primary, and it was not until one and a half years after partial removal of the tumor, which had infiltrated the meninges over one frontal lobe, that involvement of the cervical lymph nodes was noted. A specimen of the lymph nodes for biopsy at this time warranted a diagnosis of lymphosarcoma; the condition responded to treatment with high voltage roentgen rays. The patient did well for several months and has not been heard from since. We have considered this growth as a primary lymphosarcoma of the meninges, associated with secondary involvement of the cervical lymph nodes, and we have included it in the series.

One of the epidermoid cysts has been described in a report of a case by Learmonth and Kernohan,[36] as has chondroma of the falx cerebri, in a case reported by Verbrugghen and Learmonth.[37]

SUMMARY

A series of 314 microscopically verified tumors of the frontal lobes is reported on. The anatomic sites and a pathologic classification of the lesions are given.

An outstanding feature of the pathologic study is the preponderance of two types of tumor: spongioblastoma multiforme and endothelioma. These two types made up more than 70 per cent of the tumors encountered in the anterior part of the cranial cavity.

DISCUSSION

DR. RICHARD B. RICHTER: I have always believed that a knowledge of tables of findings of the kind presented is rather futile in the diagnosis of certain individual problems. I wish to ask how often it was necessary to resort to ventriculography as a means of diagnosis in differentiating these tumors, especially in differentiating lesions of the frontal fossa from those of the posterior fossa.

DR. LEWIS J. POLLOCK: While perhaps not entirely germane to tumors of the corpus callosum, but included as part of the symptomatology, there are the signs of involvement of the cerebellum. I think that the clinical neurologist should take note of the need for a clear definition of dysfunction of the cerebellum. In certain cases symptoms and signs have been observed when parts of the cerebellum have been destroyed. These have consisted of various signs, adiadokokinesis, for example. This is not necessarily a sign of disease of the cerebellum. Similarly, I have no

35. Bailey, Percival: Intracranial Sarcomatous Tumors of Leptomeningeal Origin, Arch. Surg. **18**:1359 (April) 1929.

36. Learmonth, J. R., and Kernohan, J. W.: Three Cases of Epidermoid Cyst of the Brain, S. Clin. North America **11**:853 (Aug.) 1931.

37. Verbrugghen, Adrien, and Learmonth, J. R.: Chondroma of the Falx Cerebri, J. Nerv. & Ment. Dis. **76**:463 (Nov.) 1932.

doubt that disease of parts other than the cerebellum may produce defects in cocontraction and distribution of tone of the reciprocal muscles.

The point I raise is, why should one state that in cases of supratentorial lesions there are signs referable to the cerebellum? When hemiparesis occurred in only 9 of the cases, as contrasted with the number of cases in which there were signs of involvement of the cerebellum, is it not rather a challenge to determine what defects other than those in the cerebellum produce these disturbances in motor function, rather than to attempt to explain them on some hypothetic anatomic basis? Destruction of the cerebellum as a whole does not produce signs analogous with those described. In decerebrate animals, Davis and I showed that the cerebellum acted rather as a whole in inhibiting muscle tone. I think that before they can be content to accept the view that signs and symptoms of involvement of the cerebellum occur in cases of supratentorial lesions clinicians should find a method of determining the function of the cerebellum.

DR. HAROLD C. VORIS: In answer to Dr. Richter, so far as I can determine from the records, a diagnosis was not made in any of these cases before surgical measures were instituted. The presence of a deep-seated tumor was often detected during removal of biopsy material with a trocar, but so far as I know from the records there was no diagnosis of tumor of the corpus callosum made before operation.

EFFECT OF ENDEMIC MALARIA ON THE INCIDENCE OF NEUROSYPHILIS

ROBERT J. NEEDLES, M.D.
DETROIT

Clinical and laboratory investigation in the valley of the Amazon during the past four years has led to interesting facts regarding the relation of malaria to syphilis. In this region, where malaria and syphilis are both common, neurosyphilis is not usually seen. Data have been assembled on the prevalence of both syphilis and malaria and are presented here to indicate that the widespread occurrence of the latter disease may be responsible in part for the low incidence of neurosyphilis.

The question of the mechanism by which malaria causes improvement in patients with dementia paralytica has been freely discussed. At first it was thought that something specific in the organism of malaria and in the disease that it produces benefited the victim, but as more and more reports have been published, many investigators have come to believe that the treatment depends entirely on the degree and duration of the hyperpyrexia produced and not on any specific properties inherent in malaria. The use of other types of fever therapy, such as the intravenous injection of typhoid vaccine and pyrexia produced by various physical devices, which have also given good results, has tended to strengthen the claim of nonspecificity in treatment with malaria. Indeed, Wagner-Jauregg [1] mentioned several reports in the literature of improvement in cases of dementia paralytica following febrile disease. Meyer [2] is stated to have treated dementia paralytica with suppuration of the scalp produced by a caustic ointment.

Investigators have noted from time to time that in native populations, particularly those in the tropics, dementia paralytica is rare. This situation was discussed at some length by Thom,[3] who is cited freely in regard to this condition. He pointed out that dementia paralytica occurs in the more intellectual types of persons—the brain workers. This immediately reminds one that the primitive people of no tropical country can be called intellectual. Dementia paralytica is comparatively

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1. Wagner-Jauregg, J.: The Treatment of General Paresis by Inoculation with Malaria, J. Nerv. & Ment. Dis. **55**:369 (May) 1922.

2. Meyer, E.: Die Behandlung der allgemeinen progressiven Paralyse, Berl. klin. Wchnschr. **14**:289, 1877.

3. Thom, Burton P.: Syphilis, Philadelphia, Lea & Febiger, 1922, p. 343.

rare in uncivilized peoples, but it is recognized that even among civilized countries marked differences occur in the incidence of this disease. Many countries in which it is rare are tropical or subtropical. Thus, in Sicily, the African Levant and Turkey it is stated to be infrequent. Among the uncivilized black races it is almost unknown. Most tropical countries which have little neurosyphilis have a high rate of occurrence of malaria. This coincidence has excited attention in the past.

Merzbacher and Bianchi,[4] after investigation of the incidence of malaria and syphilis in several Argentine provinces, concluded that malaria apparently modifies the evolution of syphilis in a favorable manner. This view was reiterated in a later contribution.[5] Merzbacher further stated that in certain provinces in which malaria is prevalent neurosyphilis is almost unknown. Rosenberg[6] stated that a previous attack of malaria was noted to have a beneficial effect in cases of neurosyphilis observed in tropical villages. André,[7] after three years' experience in Paraguay, noted that neurosyphilis was rare, although he did not specifically cite malaria as the reason for this low incidence. Kerim[8] in a report from Turkey stated that neurosyphilis is rare while malaria is prevalent in that country. A significant contribution is that of Kirschner and van Loon,[9] who stated in a report from Java that dementia paralytica is three times as common in Europeans as in natives. They pointed out what I consider to be an important fact, namely, that many sufferers from dementia paralytica are immune to malaria induced by inoculation. Finally, adequate attention was given by Lutrario[10] to the difference between the incidence of dementia paralytica in malarial and that in nonmalarial districts in the same country. He stated that in regions in Italy where a great deal of malaria exists there is only a small

4. Merzbacher, L., and Bianchi, A. E.: Neuetra experiencia personal respecto a la influencia de la malaria natural sobre la evolución de la sífilis nerviosa, Arch. argent. de neurol. **2**:252 (June) 1928; Estudios sobre las relaciónes entre paludismo y sífilis; efectos del paludismo natural sobre las enfermedades sifilíticas, Bol. Inst. de clín. quir. **4**:181, 1928.

5. Merzbacher, L.: Die Beziehungen der natürlichen Malaria zur Syphilis, Deutsche Ztschr. f. Nervenh. **113**:1 (April) 1930.

6. Rosenberg, M.: Die Malaria un ihren Beziehungen zu Gonorrhöe, Lues und Neurolues, Arch. f. Schiffs- u. Tropen-Hyg. **33**:463 (Sept.) 1929.

7. André, C.: A propos de la syphilis nerveuse exotique, Lyon méd. **139**:683, 1929.

8. Kerim, F.: General Paralysis and Preventive Rôle of Malaria in Syphilitic Diseases of Nervous System in Turkey, Wien. klin. Wchnschr. **39**:915 (Aug. 5) 1926.

9. Kirschner, L., and van Loon, H. F.: Malaria Treatment of General Paralysis, Klin. Wchnschr. **3**:2001 (Oct. 28) 1924.

10. Lutrario, A.: Paralysie générale et paludisme, Bull. Office internat. d'hyg. pub. **25**:1769 (Oct.) 1933.

number of cases of dementia paralytica, while the latter disease is much more common in nonmalarial regions.

Some contributors to this subject, while admitting the low incidence of neurosyphilis in tropical countries, deny the importance of endemic malaria in this situation. Thus, Mulder [11] stated that in the Netherlands Indies most natives acquire malaria at an early age, while neurosyphilis is a disease of adult life. He did not mention the recurrences which are a common part of the picture of tropical endemic malaria and which, because few natives receive adequate treatment, are numerous throughout life. Attention must also be given to the possibility that dementia paralytica is due to a neurotropic strain of the spirochete and syphilis of the tropics, to another variety. This theory is largely discounted now, and the reports of Kirschner and van Loon [9] and Lutrario [10] do not recognize a difference in spirochetal types.

Another factor which has excited comment is the rôle of arsenic therapy in the causation of dementia paralytica. There is a definite trend in the literature toward support of the belief that in the more remote parts of primitive countries, where there is little or no treatment with arsphenamine, neurosyphilis is rare. As soon, however, as arsphenamine therapy becomes more common the incidence of neurosyphilis increases. This was also pointed out to me by Cruickshank [12] as true of the British Sudan. In the valley of the Amazon the organic arsenical preparations are well known, and the native frequently asks for an injection of neoarsphenamine to relieve symptoms of any origin whatever. While these drugs are too expensive for inhabitants of the interior to use in any large amount, a considerable quantity is taken. Hence the factor of arsenic therapy would not seem to have influenced the development of the disease unfavorably.

In an attempt to clarify the relation between malaria and neurosyphilis, I am presenting data and statistics gathered during four years by the medical department of the Cia. Ford do Brasil, which is developing a rubber plantation on the Tapajos River. This river is one of the chief tributaries of the Amazon, and the properties of the company are about 600 miles (9651 kilometers) from the sea and roughly 150 miles (241 kilometers) south of the equator. The climate is tropical, with a temperature ranging from 70 to 95 F., a relative humidity of between 70 and 90 degrees and a rainfall of about 85 inches (206 cm.) a year. The native population, from a study of which these statistics are presented, is a mixture of many races. Predominant is the South American Indian, with a generous admixture of Negro and white blood. Few pure strains of any race are to be found in this region.

11. Mulder, D.: Syphilis und Metasyphilis, Deutsche Ztschr. f. Nervenh. **102**:293, 1928.

12. Cruickshank, W. B.: Personal communication to the author

INCIDENCE OF MALARIA

In tables 1, 2 and 3 are shown the results of surveys made in villages in the vicinity of the property of the company. These are typical Amazonian villages with a mixed population. It will be seen that malaria is widely prevalent, from 48 to 71 per cent of the smears being positive in these villages. In tables 4 and 5 are shown the results of surveys made on company property. Because they deal with persons living in a pro-

TABLE 1.—*Summary of Findings on Smears Obtained at Samahuma*

	No.	Percentage
Negative	1,015	41.5
P. vivax	840	34.5
P. falciparum	420	17.0
Mixed organisms	175	7.0
Total	2,450	100.0

TABLE 2.—*Summary of Findings on Smears Obtained at Itaituba*

	No.	Percentage
Negative	64	37
P. vivax	78	39
P. falciparum	52	21
Mixed organisms	6	3
Total	200	100

TABLE 3.—*Summary of Findings on Smears Obtained at Nazareth*

	No.	Percentage
Negative	190	28.5
P. vivax	243	36.2
P. falciparum	164	24.4
Mixed organisms	73	10.9
Total	670	100.0

tected zone and receiving intensive quinine therapy during relapses, these data indicate a lower incidence of malaria in this sheltered village. However, as Connor [13] pointed out, if in any survey 25 per cent of the smears are positive, it is safe to postulate that in 100 per cent of the population on which the survey was made there is malarial infection. Finally, in the four years 1930-1934, 38,786 smears were examined in the hospital laboratory in Boa Vista (table 6). It will be seen that 38 per cent of these smears were positive for one type of malaria or for several. The

13. Connor, R. C.: Annual Report, Medical Department, United Fruit Company, New York, 1931, p. 24.

commonest offender was Plasmodium vivax, and Plasmodium falciparum was next. Plasmodium malariae was so rare that it is grouped with the mixed organisms. Most natives of this part of the world acquire malaria at an early age. Quinine is costly; the natives are poor, and hence treatment is always inadequate. The victims thus fall into a state of chronic malaria and are subject to recurrences every year or so, during which occur the chills and high fever so productive of beneficial results

TABLE 4.—*Summary of Findings on Smears Obtained at Boa Vista*

	No.	Percentage
Negative	615	61.4
P. vivax	245	24.3
P. falciparum	102	10.1 38.6
Mixed organisms	43	4.2
Total	1,005	100.0

TABLE 5.—*Summary of Findings on Smears Obtained from Employees of the Company*

	No.	Percentage
Negative	1,318	67.5
P. vivax	467	23.8
P. falciparum	156	7.9 32.5
Mixed organisms	15	0.8
Total	1,956	100.0

TABLE 6.—*Findings on Smears Taken at the Boa Vista Hospital from October 1930 to July 1934*

	No.	Percentage
Negative	24,269	62.0
P. vivax	10,608	28.0
P. falciparum	3,381	8.5 38.0
Mixed organisms	504	1.5
Total	38,786	100.0

in cases of neurosyphilis. These exacerbations recur throughout life, and hence it is not fair to state that because malaria is acquired in infancy and neurosyphilis is a disease of adult life they are not related. The tremendous incidence of chronic malaria and its relation to the other members of the Amazonian pentad of disabilities have been previously discussed.[14]

14. Needles, R. J.: Health Problems in the Amazon Valley, Science **78**:532 (Dec. 8) 1933.

In summing up the facts on malaria, it can be stated, therefore, that endemic malaria is widely prevalent in the portion of Brazil from which the data for this report were obtained. In a single survey parasites were exhibited in the blood of from 30 to 70 per cent of the natives, which doubtless indicates that few go through life without one attack of fever, or several.

INCIDENCE OF SYPHILIS

Data on the occurrence of syphilis must be based on laboratory studies. Primary lesions are fairly common, but naturally they are not reliable in computing the total incidence. Tertiary lesions are so rare that one seldom sees them. True, I have performed autopsies in several cases of syphilitic aortitis, but this gives no adequate idea of the total incidence of syphilis. In table 7 are shown the results of serologic investigation. Of 6,823 precipitation tests made during four years (1930-1934), 31.8 per cent gave positive reactions. The Kahn precipitation test [15] and the flocculation test of Eagle [16] were used. The effect

TABLE 7.—*Summary of Reactions to Precipitation Tests for Syphilis*

	No.	Percentage
Negative	4,551	68.2
Positive	2,272	31.8
Total	6,823	100.0

of malaria on the results of the Kahn test was discussed by Smith [17] who in a report from Boa Vista stated that he found no effect on the accuracy of the reaction in cases of acute malaria. In a paper to be published later [18] I shall show that malaria has no effect on the accuracy of either the Kahn or the Eagle test. Hence one is justified in saying that syphilis is common in this region. Primary chancre occurs frequently, and 31.8 per cent of the serologic tests show positive reactions.

In spite of the large number of cases of syphilis in this region, neurosyphilis is rarely seen. In an experience which includes observations on more than 12,000 patients admitted to the company hospital in Boa Vista and of perhaps twice that number seen in the outpatient department and in medical inspection work, only 1 case of neurosyphilis has

15. Kahn, R. H.: The Kahn Test, Baltimore, Williams & Wilkins Company, 1928.

16. Eagle, Harry: Studies in the Serology of Syphilis: New Flocculation Test for Serum Diagnosis of Syphilis, J. Lab. & Clin. Med. **17**:787 (May) 1932.

17. Smith, C. R.: The Specificity of the Kahn Test in Malaria, J. Lab. & Clin. Med. **18**:396, 1932.

18. Needles, R. J., and Noel, W. W.: Studies in Amazonian Malaria, to be published.

been observed in which the diagnosis was proved. This was undoubtedly a case of dementia paralytica, as proved by the clinical picture, positive reactions to the Kahn and globulin tests, increased cell count of the spinal fluid and observations at autopsy. However, this patient, a white Brazilian, said that he had never had malaria, a statement corroborated by his family. Three attempts to induce malaria by inoculation with blood containing the organism were unsuccessful. At autopsy the spleen weighed only 150 Gm. This observation, I think, is significant. I am not prepared at this time to discuss splenomegaly in Amazonians, but I believe that chronic malaria is a prominent factor in causing chronic enlargement of the spleen. The spleen in this case was the only one of normal size that I observed in 85 autopsies. One may then postulate that this man was immune to malaria, and could not have those paroxysms of fever which may help in preventing neurologic manifestations of syphilis. Another case should be mentioned, which was evidently an instance of tabes. The notation was made in the early days of the plantation, before clinical laboratory facilities were available, and no serologic or histologic confirmation of the diagnosis could be made. Certainly, in the last four years only the case of dementia paralytica just cited was observed.

SUMMARY AND CONCLUSIONS

In the interior of the valley of the Amazon, as represented by the region of the Tapajos River, neurosyphilis is rare. Four years of clinical and laboratory experience with many thousands of natives has shown but 1 case. On the other hand, syphilis is extremely prevalent, and of 6,823 Kahn and Eagle tests, 31.8 per cent gave positive reactions. Malaria, likewise, is endemic, and individual surveys in native villages showed from 30 to 70 per cent positive smears, while the average percentage of positive findings for 38,786 smears examined during four years is 38 for one or more species of the parasite. It is possible that the high rate of occurrence of malaria is responsible in part for the rarity of neurosyphilis, since most natives acquire malaria in infancy or childhood and because treatment is inadequate suffer from chronic malaria with recurring acute exacerbations throughout life.

From these facts it is believed that endemic malaria influences favorably the incidence of neurosyphilis.

Clinical Notes

PALPEBROMANDIBULAR SYNKINESIS IN A PATIENT WITH ACUTE POLYNEURITIS AND FACIAL DIPLEGIA

A. M. Ornsteen, M.D., Philadelphia

In a case of acute polyneuritis with facial diplegia a peculiar abnormal involuntary associated movement was observed between the paralyzed orbicularis oculi muscles and the mandible. Each voluntary and involuntary movement of the eyelids was synchronously associated with an involuntary short, sharp movement of the jaw upward and forward, and if the mouth was held open the jaw would snap shut with a click of the teeth. The phenomenon was not reversible; i. e., movement of the mandible did not cause involuntary associated movement of the eyelids. This abnormal associated movement did not exist before the present illness, and it has since disappeared with the return of voluntary power to the face. The name palpebromandibular synkinesis is used to differentiate the phenomenon from "jaw-winking," which is known as the Marcus Gunn phenomenon. I have been unable to find a reference to a similar observation in the literature.

REPORT OF CASE

History.—On April 2, 1934, a Negro, aged 37, noticed that his face was pulled to the left and that he was unable to enunciate words clearly. In two or three days the facial asymmetry disappeared, but the dysarthria persisted. The patient had difficulty in chewing food because it collected between the cheeks and the jaws, and he noticed also that he was grinding his teeth. During the following week he suffered from pain all over the body, especially the chest. By the fifth day he was so weak that he had to remain in bed; he found walking difficult because the knees would give way and he would fall to the floor. The pain increased in intensity, and when he was admitted to the Philadelphia General Hospital on April 20 it was most severe in the hands and feet; at night he had severe headache which radiated from the right side of the mandible back over the side of the head. He described the pain in the hands and feet as a sticking sensation of increasing severity. Slight dyspnea had been noticed since the onset of the illness, and the extremities were becoming progressively weaker. There was also some difficulty in swallowing.

The patient said that he had never had a venereal disease; no history of a primary lesion was obtained. The blood was examined when he enlisted in the United States Army in 1918, but he was not given any treatment. There was no history of alcoholism. He had been married three years; the wife had had two children by a former marriage, but none by the patient. No previous illnesses were mentioned; an accident occurred five years before, with dislocation of the right ankle.

Read before the Philadelphia Neurological Society, Oct. 26, 1934.

From the neurologic service of Dr. A. M. Ornsteen at the Philadelphia General Hospital.

Physical Examination.—The patient, well developed and well nourished, was not acutely ill and in no great discomfort. His teeth were in poor condition, and gingivitis was present. The pharynx was injected. The tonsils, from which pus could be expressed, were hypertrophied and infected. The respiratory, cardiovascular and gastro-intestinal systems were normal; the blood pressure was 132 systolic and 80 diastolic. The prostate was somewhat softer than normal, and a smear was negative for gonococci. A culture from the throat was positive for Streptococcus viridans, Pneumococcus and Bacillus influenzae. A culture of the blood was sterile, and the course of the disease was afebrile.

Neurologic Examination.—There was weakness of all extremities, most marked in the legs. The patient was able to elevate the extended legs from 6 to 8 inches (15.2 to 20.3 cm.) from the level of the bed, and he could flex the knees to an angle of 120 degrees. He could raise the arms overhead and maintain them in that position, but the hand grasps were weak. Coordination in the upper extremities was good, but there was too much weakness in the lower extremities to test coordination. All tendon reflexes were absent. The only sensory abnormality when the patient entered the hospital was impaired accuracy in the sense of position of the toes. The plantar reflexes were absent; the cremasteric and abdominal reflexes were present, except the left abdominal reflex. The pupils were small, equal and regular; they reacted poorly to light but better in accommodation. The corneal reflexes were present, and there was a suggestion of slight lateral nystagmus. The eyegrounds showed slight reduction of the caliber of the arteries and normal disks. There was a slight tremor of the protruded tongue. There was complete facial diplegia of the peripheral type, and the right palpebral fissure was wider than the left. The power of the temporal and masseter muscles was good, and the jaw did not deviate laterally when the mouth was open. The soft palate moved freely without deviation of the uvula, and the gag reflex was active. There was no involvement of the third, fourth or sixth cranial nerves, nor were there symptoms of dysfunction of the auditory nerve. Facial sensation was normal.

The Palpebromandibular Motor Phenomenon: Synchronously with the ordinary blinking of the eyelids a clicking sound of the teeth was heard and a movement of the lower jaw upward and forward was observed. It was this that the patient referred to when he spoke of grinding his teeth at the beginning of the illness. By having the patient hold his mouth slightly open, the mandibular movement became exaggerated, with protrusion and slight deviation to the left side. The patient was then asked to blink his eyes voluntarily and rapidly and with as much force as he could; the blinking was accompanied by stronger movements of the mandible. On brushing the fimbria of the eyelids with the finger, thus eliciting defense blinking, the mandibular reflex also occurred. Chewing movements, protrusion, depression and lateral movements of the jaw did not cause the eyelids to blink, nor was any involuntary movement of the orbicularis muscle observed on either side.

Laboratory Studies.—The Wassermann reaction of the blood was 4 plus with cholesterolized antigen and 4 plus with the Noguchi modification; the Kahn reaction was 3 plus. The spinal fluid was clear and colorless and under a pressure of 8 mm. of mercury; the cell count was 1 lymphocyte per cubic millimeter, and there was a trace of globulin. The Wassermann reaction with cholesterolized antigen was 1 plus, and the Noguchi test was negative; the colloidal gold curve was 555554432. The blood count showed moderate secondary anemia and leukopenia, the number of cells being 5,300 on the twenty-third day of the disease and 4,300 on the fifty-sixth day.

Clinical Course.—By the twenty-first day of the illness the patient no longer complained of headache, but paresthesias of the extremities persisted and were more severe at night. He also complained of a burning sensation when the feet touched each other. The extremities became progressively weaker until he was unable to raise the knees from the bed, and he could not move the feet by the twenty-sixth day. The hand grasps were without power, but he was still able to raise the arms and keep them elevated. At this time diminution of vibratory sense was found in the lower extremities.

Improvement began in the fifth week on the left side of the face, and the patient began to flex the knees and lift them slightly from the bed. At this time there were moderate hyperesthesia and diminution of vibration in the feet and legs, and on the dorsum of the feet there were areas of hyperalgesia and tenderness. The sense of position was lost in the toes, and slight edema about the ankles and over the dorsum of the feet was noticed for the first time. Slight atrophy of the muscles of the hands and forearms was also present. The patient's ability to close the eyes continued to improve, and he could also take food with less difficulty. In the sixth week the paresthesias had disappeared, and the patient was able to raise the extended right leg about 10 cm. from the level of the bed. The left leg could be only slightly flexed at the knee but not elevated. There still was no power in the hand grasps, and atrophy of the muscles of the hands and the lower part of the forearms was increasing. At this time there was mild diminution of vibratory sense in the hands and forearms. Pain and temperature sensibilities remained intact.

In the seventh week two other abnormal associated movements were discovered, but they probably had been present though not observed because they were not sought. Lateral deviation of the eyes was accompanied by ipsilateral movement of the mandible—the oculomandibular associated movement. This was accompanied by an oculolingual movement in which the tip of the tongue moved to the ipsilateral side as the eyes were sharply moved laterally. The palpebromandibular reflex persisted throughout the illness without change, except that later the jaw snapped directly upward in the midline instead of deviating to the left. In the ninth week the patient was able to sit up in a wheel-chair, and he began to walk with assistance in the tenth week. He was discharged from the hospital three months after the onset of the illness and was able to walk haltingly with the aid of a cane. He had a fair amount of power in the lower extremities, and the strength in the upper limbs had improved almost to normal. The right knee jerk, both triceps jerks and the plantar reflexes had returned. The sense of vibration was still relatively impaired over the ankles, more on the left than on the right; sense of position was normal, and vital sensations were normally acute. The facial paralysis was improving, and the patient was beginning to draw up the corners of his mouth. The eyelids came within 1 mm. of meeting, and the palpebromandibular associated movement as well as the oculomandibular associated movement persisted.

Treatment.—Potassium iodide, 15 grains (0.972 Gm.), was given orally three times a day, the dosage being increased daily until the patient was receiving 60 grains (3.9 Gm.) three times a day; this was discontinued on the forty-sixth day. Daily intravenous injections of Pregl's solution (the solution resulting from the action of iodine on sodium carbonate) was started on the tenth day after admission in doses of 40 cc. and continued until the twenty-sixth day of hospitalization, reaching a total of 500 cc. Beginning with the twenty-seventh day of hospitalization, the patient was given 0.2 Gm. of a bismuth preparation intramuscularly twice a week, receiving nine injections in all, the therapy being terminated when the

mouth became sore. Tryparsamide, given intravenously, was begun on the fiftieth day and continued in weekly doses of 3 Gm. each. The treatment was continued after the patient left the hospital; reexamination two months after discharge showed that he had recovered considerable power in both sides of the face but with the well known associated movement between the upper and the lower branches of the facial nerve on each side. He had regained normal strength in all four extremities and was free from symptoms. All tendon reflexes were present but somewhat diminished, and vital and gnostic sensibilities were undisturbed in all parts of the body. The palpebromandibular phenomenon was not present; the oculomandibular associated movement was still observed at this time. Blinking movements of the eyelids and voluntary closure of the eyes did not produce an involuntary associated movement of the mandible but was replaced by retraction of the corners of the mouth.

COMMENT

The patient was emphatic in his denial of the existence of this symptom before the onset of the facial paralysis. His attention was called to his jaw when grinding of the teeth began on the third day following the onset of the facial paralysis. The grinding of the teeth was probably due to the reflex contraction of the muscles of mastication synchronously with the blinking movements of the eyelids. The disappearance of the abnormal associated movement after the return of power to the face is significant of its relationship to the loss of facial power. The mandibular movements were occasioned by voluntary attempts to close the eyes and by the automatic blinking movements. Impulses from the facial cortex and the striatal centers for blinking must have excited the motor nucleus of the fifth nerve to bring about the contraction of the muscles of mastication. This unusual divergence of central neuronic activity from the blocked peripheral facial pathways into the normal masticatory pathways may have its probable explanation in the preexistence of a connection between the nucleus of the seventh nerve and the nucleus of the motor branch of the fifth nerve (an anatomic hypothesis) or may be based on the preexistence of an unusually low threshold in the striatal level of vestigial association pathways between the eyes and the jaw (a phylogenetic hypothesis). The latter seems to me to be a more plausible explanation. In this regard it is interesting to note that the jaw-winking movement of Marcus Gunn has been suggested by Harman to be the survival of a movement in fishes, whereby, when the mouth is opened for breathing or eating, the gill swings open. In man the pterygoid and orbicularis oculi muscles are homologous with the deep and superficial muscles of the branchial arch of the fish's spiracle.

Carmichael and Critchley [1] described six types of associated ocular movements with other cranial nerves and considered them as "associated movements of vestigial origin and relics of purposive and more specialized movements which are to be found in the animal kingdom." They described the oculo-aural movement, which consists of rotation of the helix of each pinna toward the mastoid when the eyes are fully deviated laterally. They gave the name oculofrontalis movement to the depression of the contralateral eyebrow and the raising of the ipsilateral eyebrow on deviation of the eyes laterally. The oculolingual movement implies that the tongue points to the ipsilateral side on deviation of the eyes. The oculomandibular movement is a combined protrusion and deviation of the mandible to the contralateral side if the eyes are rapidly deviated first to one side and then to the other. An oculonasal movement is dilatation of the nostrils on extreme deviation of the eyes. In a previous paper they described an oriculostapedial movement which con-

1. Carmichael, E. A., and Critchley, M.: Brit. J. Ophth. **9**:49 (Feb.) 1925.

sists of unilateral blepharospasm with buzzing in the ipsilateral ear, which they considered to be due to an associated contraction of the stapedius muscle when the orbicularis palpebrarum muscle is in spasm.

The fact that my patient also has an oculomandibular and an oculolingual movement seems to suggest the preexistence of vestigial association pathways with a low threshold facilitating the divergence of thwarted corticofacial impulses into the masticatory pathways. With the return of voluntary facial power, the normal functional route is reestablished.

A similar phylogenetic origin may be tenable in explanation of the frequently observed blinking and tasting movements in cases of chronic epidemic encephalitis. I do not refer to the spasmodic attacks of blepharospasm which are often associated with oculogyric crises, but I have in mind cases in which there are associated blinking movements and movements of the mandible, as in tasting and chewing. Occasionally the eyelids move more rapidly when the lower jaw is actively innervated, and the jaw-winking movements are thus brought out at will. Some patients with parkinsonism, having no blepharospasm, show abnormal blinking movements when they repeatedly open and close the mouth. This is further clinical support of the intimate functional synergy between the eyelids and the mandible.

The Marcus Gunn jaw-winking phenomenon is a congenital condition and, according to Purves-Stewart,[2] generally disappears before adult life. In all descriptions of this phenomenon and its variations the mandibular movement is the active element and that of the eyelids the passive one. In my patient the reverse obtained, the movement of the eyelids being the active phase and the mandibular movement the passive one. Therefore, the term palpebromandibular synkinesis is appropriate for the phenomenon in my case, but for the Marcus Gunn phenomenon, or "jaw-winking," the term mandibulopalpebral synkinesis may be applied.

Papadato[3] described two cases of the Marcus Gunn phenomenon under the title of palpebromandibular synkinesis, but in each case there was elevation of both upper eyelids at the moment when the mandible was lowered and moved laterally. He is of the opinion that in contrast to the general view that the phenomenon is due to an irregularity in the course of some peripheral fibers passing from the nucleus of the motor branch of the trigeminus nerve to the levator palpebrae superioris muscle, there is more reason to believe that one has to deal with a phenonemnon of atavism in the motor mechanism. This statement is based on the fact that rudiments of this phenomenon may occasionally be observed in normal persons.

Coppez[4] stated that a synkinesis between the facial nerve and the motor branch of the trigeminus nerve was first described by Marin Amat under the name of Marcus Gunn's syndrome. He suggested for the condition the name Marin Amat's syndrome. Coppez observed one such case in a girl who had recovered from a refrigeration facial paralysis with a secondary contracture. When the girl was smiling a contraction of the orbicularis oculi muscle was observed; after a few successive contractions of the muscles the eye closed. During mastication, synchronous contractions of the orbicularis palpebrarum muscle was observed. Contrary to Amat's case, there was no profuse salivation or lacrimation. As to palpebral occlusion in the course of mastication, Amat assumed, Coppez continued, that part of the stimulus for the motor branch of the trigeminus nerve reached the auriculotemporal nerve; however, it is difficult to attribute to this nerve an action in the orbicularis palpebrarum muscle as no motor fibers have

2. Purves-Stewart, J.: Diagnosis of Nervous Diseases, ed. 7, St. Louis, C. V. Mosby Company, 1931, p. 219.

3. Papadato, L. L.: Sovrem. psikhonevrol. **10**:60, 1930.

4. Coppez, H.: Bull. Soc. belge d'opht. **65**:88, 1932.

been found in this nerve and its territory is relatively distant from the muscle. Such synkinesis may develop, he says, only in certain persons with a preexisting path of association; possibly the condition responsible for the synkinesis develops higher in the nuclei, where a connection between mastication and palpebral occlusion may originate.

Marin Amat,[5] in reviewing the literature with the report of the case of a child with functional synergy of mastication and elevation of the upper eyelid, made reference to a previously reported personal observation in which the inverse phenomenon of Marcus Gunn existed—the eye was almost constantly open and closed only when the mouth was opened. (This is the syndrome to which Coppez had reference.) Amat gave two hypotheses to explain the Marcus Gunn phenomenon: (1) the intervention of motor fibers arising from the masticator nerve by exercising an abnormal influence on the levator palpebrae superioris muscle, and (2) the presence of an anastomosis between the nuclei of origin of both cerebral nerves between which the functional synergy exists.

An interesting observation on a patient showing a mandibulopalpebral synkinesis was made by Zenan.[6] A middle-aged syphilitic woman had an associated movement for only two months in which smiling, chewing and talking caused clonic spasm of the right orbicularis oculi muscle. It was cured by one spinal puncture! The author reasoned that some of sort of connection existed between the motor nucleus of the fifth nerve and the nucleus of the seventh nerve, and that probably an increase of the pressure of the cerebrospinal fluid in the floor of the fourth ventricle was the factor which brought about the associated movement.

The pathogenesis of these motor phenomena, first reported by Marcus Gunn[7] in 1883, is not known owing to the fact that there are no reports of autopsy in any of these cases. Since practically all cases are congenital and associated with ptosis, it seems plausible that nuclear aplasia of the oculomotor nerve is the basic defect. Elevation of the lid, therefore, never attains cortical representation, and the absence of higher (cortical) inhibition of lower (paleostriatal) centers permits the expression of a phylogenetic associated movement between the external pterygoid muscle and the levator palpebrae superioris on the same side.

The hypothesis of some authors concerning nuclear connections between the fifth and the third nerve by abnormal fibers is not attractive, because the selection of functional synergy would not be likely to be so selective, i. e., between one muscle (levator palpebrae superioris) of the oculomotor group and one (external pterygoid) of the motor trigeminus group. This applies as well to the hypothesis of some peripheral connection between the two nerves in their course.

SUMMARY

A transitory abnormal associated movement between the eyelids and the mandible was observed during the existence of facial diplegia in a patient with syphilitic polyneuritis.

Blinking movements made the jaw snap shut, but voluntary movements of the jaw did not cause associated movements of the eyes.

With the return of facial power the palpebromandibular synkinesis disappeared.

The motor phenomenon is discussed in relation to the Marcus Gunn symptom complex, and current hypotheses are reviewed.

1613 Spruce Street.

5. Marin Amat, M.: Siglo méd. **86**:57, 1930.
6. Zenan, J.: Bull. Soc. belge d'opht. **67**:75, 1934.
7. Gunn, Marcus: Tr. Ophth. Soc. U. Kingdom **3**:283, 1882-1883.

A PITUITARY SYNDROME

Report of a Case

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Cushing [1] described a syndrome known as the basophilic syndrome of the pituitary gland, the clincal characteristics of which are: (1) adiposity of the face and trunk, usually sparing the extremities; (2) amenorrhea, or sexual impotence in the male; (3) hypertrichosis of the face and trunk (masculine in type) in females and in adolescent males, and possibly the reverse in adult males; (4) dusky or plethoric skin, with purplish lineae atrophicae, acrocyanosis, cutis marmorata and purpura-like ecchymoses; (5) vascular hypertension; (6) a tendency to polycythemia and polynucleosis; (7) osteoporosis, with softening of the bones of the skeleton and kyphosis; (8) headache, pain in the back, asthenia and fatigability; (9) hyperglycemia and albuminuria, and (10) intracranial signs, with exophthalmos, diplopia, papilledema, dimness of vision, polyphagia, polydipsia and polyuria.

Pardee [2] reported seven cases of pituitary basophilism, two of which presented the typical Cushing syndrome and five, so-called atypical or variable syndromes. The latter group consisted of cases of a mixed syndrome of intrasellar pituitary disease with evidence of neoplasm, a syndrome in which the disturbances appear to point to involvement of the suprarenal cortex, a prepubertal or pubertal basophilic syndrome and a postmenopausal basophilic syndrome.

The following case resembles those described by Pardee as cases of the prepubertal or the pubertal type. Of particular interest in this case is the fact that, in addition to the evidences of basophilic stimulation, there also exist evidences of acidophilic stimulation.

REPORT OF CASE

History.—H. N., a white girl, aged 12½ years, entered the clinic on June 20, 1932, with the complaint of weakness, nervousness, trembling spells (particularly before and during menstruation), crying, overweight and overdevelopment. The mother was living and well and had undergone a subtotal thyroidectomy eight years before. The father and one brother were living and well. The patient's weight at birth was 9 pounds (4.1 Kg.). She was small, but healthy, up to the age of 5 years. She began to grow taller at 5 years and grew normally until the age of 8 years. At 8, the tonsils and adenoids were removed. In the year following the operation the patient gained about 75 pounds (34 Kg.), her weight increasing approximately from 50 to 125 pounds (22.7 to 56.7 Kg.), and she gained greatly in height, no exact figures being available. From then on she has slowly grown taller and heavier. At the age of 11 years and 1 month she began to menstruate. The first period lasted for twenty-four days. Subsequent periods up to the present have been regular and normal, occurring every twenty-eight days and lasting four days; the amount of the flow has not been excessive. The

From the Department of Medicine, Touro Infirmary.

1. Cushing, Harvey: Further Notes on Pituitary Basophilism, J. A. M. A. **99**:281 (July 23) 1932.

2. Pardee, Irving H.: Basophilic Syndrome of the Pituitary, Arch. Neurol. & Psychiat. **31**:1007 (May) 1934.

patient had the usual diseases of childhood (chickenpox and measles), with no known complications or sequelae.

At present the patient is nervous. She cries easily and is dissatisfied. She does not play with other children, who tease her on account of her overgrowth. She complains of weakness in her limbs and trembling. The trembling is more noticeable just before and during the menstrual period. Her father becomes intoxicated practically every night and causes the family to be worried and frightened. The patient does not complain of headache. There are no difficulties with vision or hearing. She has a good appetite and eats a great amount. She does not suffer from indigestion, and bowel movements occur regularly. Occasionally she has nocturnal enuresis. She has advanced in school work normally. There has been no excessive drinking of water, polyuria, nocturia or frequency of burning in urination. She is too fat and too tall for her age.

Physical Examination.—When the patient was 12½ years of age the weight was 150½ pounds (68.2 Kg.); the pulse rate, 128; the blood pressure, 142 systolic and 80 diastolic; the temperature, 99.2 F., and the height, 62 inches (157.48 cm.).

TABLE 1.—*Data for Patient During Period of Study*

Date	Weight, Pounds	Basal Metabolic Rate	Pulse Rate	Blood Pressure	Age		Height, Inches
					Years	Months	
6/30/32	150.5	....	128	142/80	12	9	62
7/ 2/32	149.5	....	132				
7/22/32	149.5	+27	148	144/60	12	10	62
8/21/33	154.0	+ 4	140	146/66	13	11	63.5
11/22/33	156.0	+18	110	122/78	14	2	63.5
12/ 1/33	160.0	....	104				
12/ 8/33	158.5	....	108	128/74			
3/23/34	156.0	....	100	122/70	14	6	63.75
4/ 1/34	.....	....	88	114/72			

The pupils reacted to light and in accommodation. The ears were normal. The mouth and throat presented no abnormal findings. There was symmetrical enlargement of the anterior part of the neck, which was considered to be due to moderate, diffuse enlargement of the thyroid gland. The breasts were large and nonsecreting. There was only a scant growth of axillary hair. There was a fine tremor of the fingers. The heart and lungs were normal, except that there was tachycardia. The abdomen presented no abnormal findings (striae were not looked for at the first examination). The pubic hair was of female distribution and abundant. The extremities presented no abnormal findings. There was generalized obesity, particularly of the chest, abdomen, buttocks and thighs.

Laboratory Examination.—The urine was normal. The Wassermann test was negative. The blood count was as follows: red cells, 4,100,000; hemoglobin, 70 per cent; white cells, 24,000, and neutrophils, 80 per cent.

The cardiac rate was 115 per minute. An electrocardiogram showed slight slurring of the QRS deflection in the first lead, a PR interval of 0.12 second, sinus tachycardia and a QRS interval of 0.07 second.

The basal metabolic rate was +27 on July 22.

Course.—The patient did not return to the clinic until August 1933. The original and subsequent findings are summarized in table 1.

In table 2 the relationship between the normal variations in height and weight and the variation in the height and weight of the patient are summarized.

On August 21 a roentgenographic examination (Dr. Rodick) of the skull and sella turcica revealed the following: "Examination of the skull shows all of the structures within normal limits. The sella turcica is considered to be normal in size, and there is no evidence of erosion."

On August 15 the blood sugar during fasting was 91 mg. per hundred cubic centimeters. The morning temperature at 10:30 was 99.4 F.

On March 28, 1934, the roentgenologist made the following report: "Examination of the left elbow shows all of the epiphyses now fused with their respective shafts."

On April 4 the roentgenographic report was as follows: "Examination of the hand and wrist shows all of the epiphyses of the phalanges and metacarpals to be united with the shaft. All of the carpal bones are well formed, but the epiphyses of the radius and ulna are not entirely fused; this corresponds to an age between 19 and 20 years." (The patient's actual age at this time was 14½ years.)

TABLE 2.—*Comparison of Normal Variations in Height and Weight with Variations in Height and Weight of the Patient* *

Age, Years	Normal				Patient	
	Height, Inches		Weight, Pounds		Height, Inches	Weight, Pounds
	Minimum	Maximum	Minimum	Maximum		
12	55.6	59.6	70.7	90.5		
12½	56.7	60.7	74.5	95.7	62.00	150.5
13	57.7	61.7	78.7	101.7		
13½	58.5	62.7	83.6	107.2		
14	59.3	63.5	89.3	113.5	63.50	156.0
14½	59.9	64.1	92.4	116.6	63.75	156.0
15	60.4	64.6	95.7	119.7		

* The normal variations (for females) are from Engelbach.

On March 23 the patient was referred to the ophthalmic clinic for examination of the eyegrounds, which proved to be normal. On March 28 examination (Dr. Weems) showed that the "visual fields for form and color are normal in extent."

Reexamination on March 23 revealed, in addition to the findings summarized in table 1, an absence of hirsuties, while numerous abdominal striae were present on the flanks, the color of which was not purplish, but light pink, closely resembling the color of the skin.

No treatment was given at any time during the observation, except occasionally a mild sedative.

The obvious tendency in this patient has been from hyperfunction toward normality. Whether the trend will continue into hypofunction remains to be seen. It is also to be noted that any early gigantism was held within normal limits by markedly early closure of the epiphyses.

COMMENT

This patient resembles the one in Cushing's [1] case 14 (pituitary basophilism), in whom precocious adolescence was followed by amenorrhea, hypertrichosis, acrocyanosis, the appearance of purplish abdominal striae and vascular hypertension. However, the basal metabolic rates were low (—28 and —33) as opposed to the

increased rates in my case, and the epiphyses united normally, while in my patient greatly advanced union is in evidence. In my patient hypertrichosis and acrocyanosis were absent.

My case also bears certain resemblances to Pardee's cases 6 and 7.

It is considered that in my patient several of the elements of the anterior lobe were hyperfunctioning, producing precocious adolescence, overgrowth, hypertension, tachycardia, increased basal metabolic rates, early epiphyseal union and obesity. These were considered to be the results of primary hyperfunction of the anterior lobe and secondary overstimulation of the thyroid and gonads and possibly of the adrenal glands.

A tumor of diagnostic size evidently did not exist in the pituitary gland, as no evidence of pressure was found. It is possible that a basophilic adenoma exists with hyperplasia of the remainder of the anterior lobe, as Cushing has shown can occur, or that there is more or less complete hyperplasia of the anterior lobe.

In this connection, Cushing's discussion of Pardee's paper is pertinent: "Certainly the more that is learned about it [basophilic syndrome], the less inclination there will be to divide it into clinical subtypes. . . . All pituitary disorders, are, of course, symptomatically polyglandular, and the variable degree in which they secondarily derange the parathyroid, suprarenal, thyroid glands and pancreatic islets will serve to modify the clinical picture."

Acidophilism (overgrowth of stature and early epiphyseal union) has not been described as occurring with basophilism, but in this case there are undoubtedly evidences of both existing in the same patient.

SUMMARY

A case presenting a pituitary syndrome is reported in which it is considered that hyperfunction of the anterior lobe of the pituitary gland has occurred. The actual pathologic change in the gland remains undetermined. Evidences of both basophilic and acidophilic stimulation are present in the patient.

SPECIAL ARTICLES

HARVEY CUSHING

HAROLD ELLIOTT, B.Sc.
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The fourth Cushing in direct line to pursue a medical career with distinction is Harvey Williams. His great-grandfather, David Cushing, had practiced medicine in Berkshire Co., Mass. His grandfather, Erastus, after graduating from the Berkshire Medical College in 1824, had moved west in search of a less rigorous climate and settled in Cleveland. The eldest of the sons of Erastus, Henry Kirke Cushing, was graduated in medicine from the University of Pennsylvania. Henry returned to Cleveland to help his father with his practice and in time was elected to the chair of obstetrics and gynecology at the local university of the Western Reserve. After his return to Cleveland he married Betsey Williams of that city. The Williams family had also migrated from Connecticut at a time when Cleveland was only a village on the Cuyahoga River. They had settled in the district known as the Western Reserve of Connecticut, later incorporated into the state of Ohio.

To Henry and Betsey Cushing were born nine children, the last of whom is the subject of this biographical sketch. Of his boyhood in Cleveland one gains a glimpse: Harvey accompanying his distinguished father to the Case Library. There his father would enter the corner of the library (which was wired off and barred to all but those privileged physicians who possessed a key) to bury himself in the latest copy of the London *Lancet*. Meanwhile, the son betook himself to a deep window-seat outside the wire enclosure, whence he could command a view of the old public square beyond. From this association it seems fair to surmise that the son can thank environment as well as inheritance for the impulse that eventually sent him into a career of scholastic medicine.

Harvey went to college at Yale, where he played baseball with great enthusiasm and incidentally came under the influence of Russell H. Chittenden, the physiologist and biochemist. He was graduated from Yale in due course and entered Harvard Medical School, following the example of his elder brother Edward, from which in 1895 he received the degree both of Master of Arts and of Doctor of Medicine.

"The medical traditions of my forebears," wrote Cushing, "inclined me to the abnegating life of a family practitioner. To this I looked forward during my medical course in the early nineties. . . ." [1] Once again following the example of his brother, he entered the Massachusetts General Hospital as surgical intern and was attached to the newly established south wing. It is interesting to quote from Cushing's description of the surgery of his days of internship.

> A good deal of it, to be sure, in the retrospect appears somewhat old fashioned and we were misled in many ways. We operated too much by the clock; the wealth of material was still utilized in no way except for added experience; cases were insufficiently studied before operation; our fracture dressings were so neat and laboriously made we would hesitate to take them down to see if all was well beneath.[2]
>
> Such minor operations as were recommended were largely orthopedic in nature, and though the skull might often enough be trephined for fracture, I saw as a hospital intern in surgery only one operation that I remember for an organic lesion in the brain.[1] A patient with Jacksonian epilepsy having a "march" involving the upper extremity was sent into the hospital for operation, by the professor of neurology. After repeated craniocerebral measurements the situation of the chief fissures was marked with an indelible pencil on the shaven scalp, the precise spot overlying the center whence movements of the thumb were presumed to originate being indicated by a cross. At this spot the surgeon, into whose service the case had come, was expected to trephine, and on the eventful day, through a stellate incision he removed a button of bone about an inch in diameter. A discussion ensued as to whether the tense dura which had been exposed should be incised, a step which was finally taken without disclosing a recognizable lesion. This negative finding was looked on as rather a joke on the neurologist, who, poor man, had assumed the entire responsibility, and there seemed no reason for any further surgical interest in the matter.
>
> This was a typical example of surgery made to order, a relic of medievalism in medicine brought down to the end of the nineteenth century.[1]

Another anecdote of those days is as follows:

> In the spring of 1896 when I was a house officer, Dr. J. C. Warren, then professor of surgery in the Harvard Medical School, came back from Roentgen's laboratory and showed us a shadow picture of the human hand in which the outlines of the bones were apparent. He showed us, too, a mysterious glass tube about as big as an orange with which the picture had been taken. It of course aroused the greatest possible interest. E. A. Codman and I with the help of Walter Dodd, the hospital pharmacist, who knew something of photography, immediately began to see what we could do in the way of getting similar pictures. This, I suppose, is nothing more than what happened in many other parts of the country at about the same time.[3]

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1. Cushing, Harvey: Neurological Surgeons: With the Report of One Case, Arch. Neurol. & Psychiat. **10**:381 (Oct.) 1923.

2. The Personality of a Hospital (Ether Day address, Massachusetts General Hospital, Oct. 18, 1921), Boston M. & S. J. **185**:529 (Nov. 3) 1921.

3. Cushing, in discussion on Sosman, M. C., and Putnam, Tracy J.: Roentgenological Aspects of Brain Tumors: Meningiomas, Am. J. Roentgenol. **13**:10, 1925.

In the autumn of 1896 Cushing went to Baltimore as junior assistant in the surgical service of Professor Halsted. What a place for a young man with insight and enthusiasm was the Johns Hopkins Hospital, then in the first decade of its existence! The creators of that great institution were still its leaders and young enough to fire their chosen assistants with their own spirit: Welsh, Halsted, Osler, Mall, Abel, Howell and Kelly. Halsted—called "the professor" by his assistants—was a scholarly, shy man of delicate perceptions and a habit of making searching inquiry into the physiologic principles which underlay surgical problems. He translated some of his conclusions into progressive refinements of

HARVEY CUSHING

surgical technic: the use of rubber gloves and fine silk and fastidious gentleness in the handling of tissues. These were some of the technical traditions which Halsted communicated to his pupils, who form what may now be called a Halsted school of surgery. The same refinements of technic may be detected in the work of the even more numerous pupils of Harvey Cushing.

Thus Cushing was stimulated by the teaching of America's most distinguished surgeon, but it is probably no less important that he also came under the spell of that scholar in medicine William Osler. Certain qualities in his writing and certain cordial mannerisms betray the influence which Osler must have exerted. Indeed, Cushing lived for some time at 3 West Franklin Street next door to the Osler house, with

a group of Oslerian satellites called the "latch-keyers" because of their constant intimacy with the Osler household.

On his arrival in Baltimore Cushing's interest in roentgen ray photography was unabated, and he made the first roentgenograms that were made at the Johns Hopkins Hospital, "with the aid of a decrepit and perverse static machine, as big as a hurdy-gurdy and operated in the same way—by turning a crank." [3] His first paper submitted for publication contained an account of a case of gunshot wound of the spine with plates showing the location of the bullet.

Cushing wrote:

> . . . And though at the time I was much more absorbed in Roentgen's recent discovery than in neurology, and had never before heard of hematomyelia, for the next six months with such precision as I could master I plotted out her anesthetic skin fields and followed daily with accumulating interest her subsiding paralyses.
>
> This opportunity personally to study for the first time a neurologic case, which though a nonoperative one had drifted into and was permitted to remain in a surgical ward, made a great impression on me, and spurred on by H. M. Thomas and L. F. Barker, with the report of this case I started on my inky way.[1]

For four years Cushing carried his part of the burden of a general surgical clinic and made experimental studies of the production of gallstones, the bacteriology of the alimentary canal and the development of cocaine anesthesia.

In 1900 his interest had turned toward the field of the nervous system, and he went abroad for a year of study, crossing the ocean on the same boat and in the same cabin with Osler and Thomas McCrae, then resident physician at "the Hopkins." On arrival in England Osler delivered an address which he entitled "The Importance of Post-Graduate Study." [4] He recommended this activity as an antidote against premature senility. He concluded the address as follows: "I predict that in the twentieth century the young English physicians will find their keenest inspiration in the land of the setting sun."

Cushing went first to London,

> Where I found Horsley kindness itself, but despite an insatiable craving for research his time had become so taken up with a large consulting practice, with the development of his general surgical service at the University College Hospital, as well as with matters relating to professional politics, that most of his investigative work was done at odd hours at his home.[1]

Consequently the young surgeon with vague talk of returning for some work later drifted over to France and finally to Switzerland, where in Bern he spent a most engrossing year in Kronecker's laboratory.

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4. Osler, William: An Address on the Importance of Post Graduate Study, Lancet **2**:73 (July 14) 1900.

He undertook a problem suggested by Kocher, namely, the physiologic relationships of intracranial tension. As a result of the work Cushing pointed out along with many other things that the systemic blood pressure rises as the result of a dangerous increase in intracranial pressure. In the spring he started south and continued the work on intracranial tension in the physiologic laboratory of Professor Mosso in Turin.

From Italy Cushing went to Liverpool and spent four months there with Prof. Charles Sherrington, whom he assisted in some of his celebrated experiments with Grünbaum on the delimitation of the motor cortex of anthropoids. During the course of the experiments he made some drawings of the cortex, which betrayed his unusual talent as an artist. Before he began his practical work as neurosurgeon his only experience of the central nervous system was through the medium of experimentation on animals. In that respect his preliminary preparation was similar to that of Horsley.

Thus equipped, Cushing wrote:

> . . . I returned to Baltimore (late in the autumn of 1901) and petitioned for a post as neurosurgeon in the clinic.
>
> My former chief was evidently staggered at the proposal. He suggested as an alternative that I take a position in orthopedics, a subject which in his opinion covered practically all neurologic maladies having surgical bearings. . . . Consequently, for the next few years I continued to do general surgery in an adjacent hospital, and contrary to all expectations, neurologic cases began to accumulate in such numbers as to guarantee a living.[1]

In 1902 he married Katherine Stone Crowell of Cleveland, whom he had known from childhood. Dr. and Mrs. Cushing came to live at 3 West Franklin Street in Baltimore, which they shared with Dr. T. B. Futcher, the other "latch-keyers" having married themselves away.

From 1901 to 1913 Cushing remained in Baltimore. He dominated the experimental work of the Hunterian Laboratory and developed a splendid teaching course in surgical anatomy, using animals as subjects. In referring to Cushing during these years Crowe said: "I do not recall that he was ever sick although he worked harder, more hours each day and more days out of the year than any man I have ever known."[5] Most important of all, during these years he labored to create a special field in surgery, that of neurosurgery. He was satisfied with nothing short of perfection in each surgical procedure and demanded the same high standard of all associated with him. Most of the cranial operations at the beginning were miserable failures. After long hours of heartbreaking effort he would have to face the fact of the patient's death. A more easily quenched spirit would have taken "no" for an answer, would have concluded that "the professor" was

5. Crowe, S.: Personal communication to the authors, August 1934.

right, that this was not a field for specialization. But Cushing was dauntless, and gradually successes made their appearance. Patients were saved who had been facing certain death, and others who had resigned themselves to unrelievable pain were cured. Cushing's fame spread, and the sufferers from neurologic ailments began to flock to him.

At this time Cushing did pioneer work in studies of blood pressure in man. He developed and described the subtemporal decompressive operation. He applied himself to perfecting hemostasis and devised a clamp by which to apply a small silver clip to bleeding vessels on the brain. Perhaps more important than any other of his technical elaborations, he recognized that in closure of the scalp the galea or deeper fascial layer must be sutured carefully as a separate layer, and for this he used fine silk, so that the healing of his incisions was unrivaled and leakage of cerebrospinal fluid was prevented.

At that time, as always, Cushing's chief preoccupation was with the physiology which lay beneath clinical manifestations. He observed fluid "weeping" from the human choroid plexus in the opened ventricle, charted sensory as well as motor areas of the cortex of patients under local anesthesia and began two chief lines of laboratory investigation: first, the physiology of cerebrospinal fluid, and, second, the physiology of the pituitary body. Some of the work in these two fields he did alone; some he did with the help of his pupils, and some was carried out by his pupils alone, along the line of his original conception.

In 1912 Cushing accepted a call to Boston, where he became Moseley Professor of Surgery at Harvard and surgeon-in-chief to the Peter Bent Brigham Hospital. This hospital, though not quite completed, was opened formally in April 1913 with addresses by Prof. John Collins Warren and Sir William Osler, then Regius Professor of Medicine at Oxford. The foundation of the Arthur Tracy Cabot Fellowship made it possible for the professor of surgery to put a full time worker in charge of experimental surgery in the Warren Laboratory of the Harvard Medical School, and Cushing filled this position with a succession of brilliant assistants, beginning with Lewis Weed.

In August 1913 Cushing attended the memorable International Medical Congress in London, where he gave the surgical address on "Realignments in Greater Medicine." Kocher escorted his erstwhile pupil to the platform. "Dr. Pound of Cure Lane," said Cushing, "is being superseded by his young disciple Dr. Ounce of Prevention Street." [6]

But the Great War was at hand. It put an end to thoughtful, creative work, and these years may be passed over quickly. Cushing threw him-

6. Cushing, Harvey: Realignments in Greater Medicine: Their Effect upon Surgery and the Influence of Surgery upon Them, Brit. M. J. **2**:290 (Aug. 9) 1913.

self into the struggle before the United States declared war and served with distinction in the British Expeditionary Force. He became surgical director of the United States Base Hospital Number 5 and was appointed senior consultant in neurologic surgery to the American Expeditionary Forces with the rank of colonel. He received many honors: D. S. M. (U. S.), Companion of the Bath, Officer of the Legion of Honor and others. And yet it cannot be said that his career was greatly forwarded during the war. At best, war served as an interlude. Selections from his diaries of the war period have appeared in the *Atlantic Monthly*. He returned to Boston in 1919, suffering from peripheral neuritis, to take up his work where he had laid it down at the Peter Bent Brigham Hospital.

Sir Victor Horsley also had dropped his tools and gone to war, but, like many a younger man, he never returned. War brought him only sudden silence, the close of a career before the fire of enthusiasm had waned. Cushing could never, of course, be called a pupil of Horsley, and yet he became in many ways his successor. The two men differed so much in character and in their approach to surgery and research that they may not be compared.

During the fifteen years from 1919 to 1933 Cushing worked indefatigably in his clinic in Boston. He gathered books from far and near for his personal library and acquired an almost complete collection of the writings of Vesalius. He developed a high degree of perfection in operative team-work. His case records became available storehouses of clinical observation. Without depending on neurologic consultation he made his own studies of every case and described with great clarity the syndrome which accompanies the growth of various types of tumors in the cranium and in the sella turcica.

The low annual mortality which he was able to report reveals how far he had advanced his specialty, and young surgeons flocked to him from all over the world. The result is that today almost every great city in Europe and America has one or more pupils of Cushing devoting themselves with distinction to the specialty of neurosurgery. The migration of medical students for their "wander-years" had been traditionally from west to east, from the new world to the old. Cushing inaugurated the reversal of this migration, which Osler had prophesied.

In 1919, after the death of Sir William, Lady Osler turned to Cushing for the authorship of her husband's biography. Cushing had buried her only son, Revere, in France, and with him the heart of his father, and now it was to be Cushing who should gather up the multitude of Osler's memories, scattered as they were through the world, and preserve them from oblivion.

Quietly and without relaxing the incessant routine of his operative clinic Cushing began the enormous task of collecting the material for

this biography. He worked in the early morning at home, arriving at the hospital at ten or eleven, where he was apt to plunge into a major operation at once. For from three to six hours he would operate with the utmost concentration, never lifting his eyes from the operative field. Complete silence reigned in that operating theater in spite of the fact that the stand was usually filled with distinguished visiting physicians. When the operation was over he withdrew to a tiny dressing-room, where a faithful orderly prepared tea and toast and where he dictated full notes of the operation and made one or more drawings of the operative field with the deft, quick hand of the artist. There followed voluminous correspondence, dressings, rounds with his resident surgeon and a little time in the pathology laboratory. Some days he wore his operating uniform until evening. The whole clinic responded to the steady pressure of the tireless hand of the chief, and as time passed that hand delegated less of his own work to his assistants, not more.

The biography of Osler appeared in 1925 in two large volumes. A great effort had evidently been made by the author to preserve here all of the biographic material entrusted to him even at the risk of prolixity, and yet Cushing completely effaced himself from the picture so that only those who had been themselves behind the scene could perceive how often he was an unnamed actor on the stage. His "Life of Sir William Osler" was awarded the Pulitzer prize as the best biographic writing of the year, a monument to the memory of Osler, a testament to their friendship and a lasting tribute to the scholarly attainment of the biographer.

In 1932 Cushing retired from his posts in Boston, at a time when he was working at the height of his power. His operative results in the last year eclipsed anything he had ever achieved before, mortality having dropped to about 5 per cent. Nor had there been any slackening in his other manifold activities when he accepted a call to Yale, the university of his undergraduate days, to become the Sterling Professor of Neurology.

This account should not presume to assess the value of the past scientific contributions of Cushing any more than it should attempt to predict the importance of the work that he will in the future carry out at Yale. Posterity gradually sifts gold from gravel in the pan of time, and what seems to be of contemporary importance may be "fool's gold," while the seeming incidental may prove a heavy nugget. But even when his scientific contributions are ignored, it is obvious that Cushing in his own practice raised neurosurgery to its highest level of perfection. Under his inspiration a dynamic school of neurosurgeons has come into existence. Neurophysiologist, scholar and surgeon in the true tradition of William Halsted, he is worthy of a permanent place in neurology's Hall of Fame.

SILAS WEIR MITCHELL
1829-1914

OLAN HYNDMAN, M.D.
AND
WILLIAM CONE, M.D.
MONTREAL, CANADA

The many-sided personality of Silas Weir Mitchell found its expression in different directions like light from multiple facets. He made a brilliant success in two major fields of activity, first, medicine, in particular neurology, and, second, literature. More difficult to evaluate were his contributions to other activities, such as public affairs and hospital management. But shining through the record of all his activities was his warm humanity, his stimulating influence on his many associates and his unfailing effort to relieve human suffering in any form. He loved to live and to contribute. One of his colleagues has said that Walter Savage Landor's words, "I warmed both hands before the fire of life," were more true of Mitchell than of any other man he had known.

Weir Mitchell was born in 1829, of Scotch descent. It is of interest that his great-grandfather, Collector Mitchell, was a friend and companion of Robert Burns. His father was his affectionate chaperon. He prepared him physically with outdoor activity and was the "best physician he ever knew." Indeed he was a distinguished physician and Mitchell's greatest educative influence.

Mitchell's early education did not portend genius. He was bored with laborious study and absorbed rather than applied himself to studies. His father said: "You are wanting in nearly all the qualities that go to make success in medicine. You have brains enough but no industry." Mitchell later said: "He was correct enough. I developed late."

His medical education was not remarkable. He left the University of Pennsylvania in 1848 before completing the senior year in the undergraduate college, went to Jefferson Medical School and graduated in two years (at the age of 21). The teachers, in spite of the poor medical curriculum of the day, were of the caliber to produce good results.

A year of medical study in Paris broadened Mitchell, and though he tried faithfully to fulfil his father's wishes and become a surgeon, he liked better the lessons of Bernard in physiology and of Robin in microscopy. He later said: "I fainted so often at operations that I began to despair, but finally overcame my horror of blood and pain."

His ambition was to win a place in physiology, and he began immediately his researches in physiology, comparative anatomy and toxicology. Prof. Samuel Jackson earnestly advised him to forsake experimental physiology if he wished to practice medicine, but Mitchell refused the advice and pleaded strongly against it until changed medical practices made the plea unnecessary. His career was based on what is now called investigative work. When a snake vendor came to his house with a box of rattlesnakes Mitchell did the unexpected thing and bought them. The study of snake venom occupied him for half a century, and out of it came, as Welch has said, an epoch-making work on the toxic albumins of snake venom and on plant and bacterial toxins. This work was carried out in association with Moorhouse and Reichert and inspired Flexner and Noguchi's fine volume on snake venoms. "If," as Welch said, "it be true that he developed late, then surely by twenty-eight he had fully arrived."

The turning-point in his career came in 1863, when he assumed medical charge of an army hospital for patients with nervous diseases. Preceding this he published not less than 22 medical papers and reports, all the result of personal research work. He observed the production of cataract in the frog by the ingestion of cane sugar, the effect of mechanical stimulation of muscle, the nerve chiasm on the larynx of turtles, the insusceptibility of pigeons to morphine and certain effects of freezing parts of the central nervous system.

After 1863 came his work in clinical neurology. However, even then he published at least 10 physiologic and about 25 pharmacologic and toxicologic papers. His researches were chiefly in the field of neurophysiology, among which were contributions on the physiology of the cerebellum (views that were later advocated by Luciani). Reports on cutaneous sensation in cases of injuries of nerves embodied principles, including that of overlapping, and observations later elaborated by Head and Rivers in their work on protopathic and epicritic sensation. Researches on tendon and muscle jerks, the observation of crossed thermal sense and views on fatigue and exhaustion of nerve cells as a result of peripheral irritation were some of the contributions to neurophysiology and neuropathology which led Howell to state that previous to the work in the laboratories of Bowditch and Newell Martin the most significant work from the standpoint of physiologic investigation was that of Weir Mitchell. Mitchell suggested the creation of the American Physiological Society and with Bowditch and Martin called its first meeting.

During the Civil War Mitchell suggested the establishment of the hospital for nervous diseases and injuries located in Turner's Lane, Philadelphia, and appointed W. W. Keen, his most devoted co-worker, as junior assistant. These two, with Moorhouse, worked indefatigably

and recorded everything. A series of publications followed, among which were "Gunshot Wounds and Other Injuries of the Nerves," "On Malingering," "On Antagonism of Morphia and Atropia" and the study which some consider his most important contribution to neurology, "Injuries to Nerves and Their Consequences," which Welch thought to be comparable with the reports of Duchenne and Charcot on diseases of the spinal cord.

After the war Mitchell became the leading neurologist in America. Keen spoke of him as having been the most remarkable medical man he had ever known in Europe or America and said: "I owe to him the path I have trodden, the literary and scientific impulse I have received and any success I may have achieved." Sir James Paget once remarked to Keen: "Mitchell is one of the most distinguished medical men in your country," adding after a pause, "or in any country." His conviction in this was borne out by advising many Americans who crossed the Atlantic to return to consult Mitchell.

In 1870 Mitchell was instrumental in establishing the Infirmary for Nervous Diseases as a part of the Orthopaedic Hospital, where for over forty years he led a school of able men who have brought renown to American medicine.

This brief space is not sufficient for the complete enumeration of Mitchell's original observations in neurology, some of which were: "Postparalytic Chorea," "Erythromelalgia" (Mitchell's Disease), "The Reflex Disorders Due to Eye Strain," "The Unilateral Hard Oedema of Hysterical Hemiplegia," "Relation of Pain and Weather," "Forms of Neuritis" and "Trophic Disorders and Causalgia." Welch collected 246 references, 119 on neurology, 52 on the preclinical medical subjects and the remainder historical, biographic, etc.

While Mitchell's brilliant mind and aptitude for science sharpened his skill as an investigator and diagnostician, his affection and sympathy for suffering humanity stimulated a profound interest in therapeutics. In this field also he made important contributions. Chief among these is the so-called "Rest Treatment," and obvious as such therapy now seems, it was met during its inception with as much adverse criticism as was Paré's introduction of the simple ligature. Mitchell recommended amyl nitrite to abort epilepsy and ice and sprays to reduce pain and spasm. He was among the first to use massage and faradic current therapy and to suggest section of nerves and stretching of nerves. In 1884 he served with H. C. Wood as consultant to the department for the insane of the Philadelphia Hospital, where he expanded the crowded quarters and remedied other shortcomings so as to give greater comfort.

Although Mitchell never occupied a chair in any medical school he was, as Dr. Frederick P. Henry said, through participation in medical

societies, the teacher of those who taught. Twice he failed to be appointed to a chair of physiology for which he was a candidate, but, as Osler said, it was probably an advantage never to have been hampered by academic harness.

He frequently rendered financial assistance to younger men in their struggle for success in early professional life. He quietly arranged direct loans, unsolicited though they might be. He often advanced sums to assist in their research or paid them for literary work or for professional assistance. A letter to Osler in 1913 (the next to his last letter) contains the following statement: "Noguchi's splendid discovery pleases me greatly, who picked him up a starving Japanese some twelve years ago and secured him means of living work." It was Weir Mitchell who was commissioned by the trustees of the University of Pennsylvania to "look Osler over" as a possible successor to William Pepper and who the next day cabled "All right. Elect Osler."

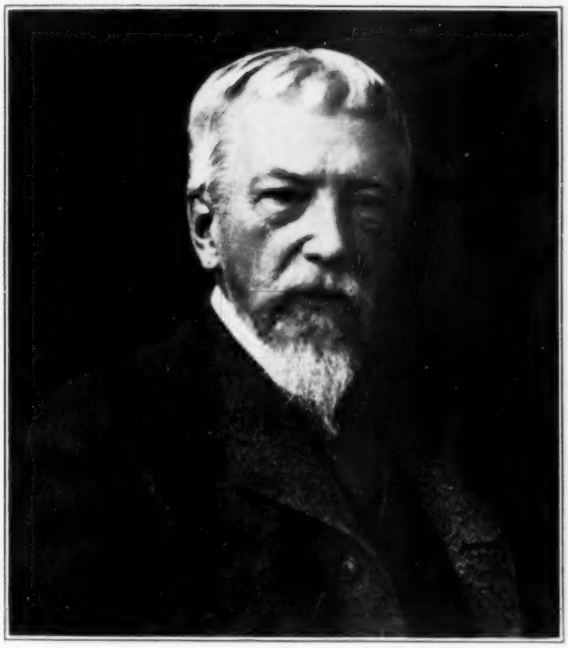
Mitchell himself began as a poor man, rich only in his family heritage. He was the seventh physician in three generations, and the phrase "south of Market Street person," so significant then in Philadelphia society, applied to him. The receipts during the first ten years of his practice were meager. He was faced with the burden of his father's family and his own approaching marriage. Yet he found time for laboratory work, and in 1858 at the Academy of Natural Sciences (to which he was elected in 1853) he presented the first paper at the first meeting of the section of biology, "Blood Crystals of the Sturgeon." He did develop a lucrative practice, however, and in later years the income from his pen was as great as that from his professional activities. He donated substantially to libraries and societies and said that he parted with half his income that he might enjoy the kingdom of the mind.

If any one of his societies was his best love it was the Philadelphia College of Physicians. In fifty-eight years' service to it he was twice elected president, Da Costa being the only other member to share such honor. He was a great believer in a good dinner and good company and gave a fund to the college to promote fellowship by an annual festival. His reputation for sociability and conviviality was widespread. On the event of his death in 1914 a special meeting was called by this society, and a series of obituaries was given that not only recorded the plaudits due a great man but expressed a deep affection and feeling of personal loss on the part of such men as James Wilson, Keen, Tyson, de Schweinitz, Frederick Henry, Talcott, Williams, Welch and Owen Wister.

Many honors were bestowed on him both at home and abroad. In a catalog of his scientific and literary work Osler inserted the following note: "I have brought S. W. M.'s name before the Council of the Royal Society as a candidate for foreign member. The election takes place

next month and the contest will be between Mitchell and Ehrlich." He later added in brackets, "M. was elected."

Not to give consideration to Mitchell's genius for literature would be like holding a smoked glass before the sun, for it was through prose and verse that he expressed much of his profound philosophy and deep insight into human life. His novels were many and often contained a medical setting. "Hugh Wynne" has been considered the best. The novels and his verse rank high as permanent examples of the best American literature. Some have considered his "Ode on a Lycian Tomb" his best verse. The "Lycian Tomb" or "Les Pleureuses" is a



SILAS WEIR MITCHELL

famous monument in the museum at Istanbul composed of eighteen figures in different attitudes of grief. The ode was written in memoriam after the death of his daughter Maria Gouverneur Mitchell, and as he stood grief-stricken before the tomb it is characteristic that he did not think of himself alone but was preoccupied with the grief of all mankind. He was not an agnostic. He maintained his simple Presbyterian faith but doubted whether any hereafter could be sweeter than life on "our own old earth . . . companioned by the mighty dead" and by one's loved ones.

One sees Mitchell at this time (1898) in excellent physical condition, somewhat taller than the average but slightly stooped, with smiling gray

eyes, white hair and beard. His distinctive appearance and manner of speech were in keeping with his brilliant character.

He corresponded regularly with Osler, many of his letters being written by hand. His later ones reveal a tremor which he attributed to smoking large black cigars, but which to him were worth the complications. His letters revealed an intensive interest in the life of Harvey, who was always his ideal. Even when past 80 his humor and wit sparkled. The following quotations reveal it to some extent:

> I have seven reasons to refuse to speak at the unveiling of Rush. . . . Remember whenever you come this way, the board is low, the company questionable, the cellar good.
>
> January 1911: I have resigned my trustee-ship at the University after thirty-five years' service. There is the usual constant hot weather in the faculty and I believe this is the case wherever doctors are associated together in teaching positions. What causes it?
>
> Getting out of the University relieves me of Committees. In fact I have said to my wife if I died she must put over my grave "Committeed to the grave."

On Nov. 29, 1913, his son John's horse had fallen, injuring him badly, so Mitchell asked that he be relieved from his work in the hospital for the winter. In the next to his last letter he wrote: "You may imagine what this is to me, knowing as you do the unusual affection which binds us together; there is rarely so perfect a tie as in the case of John and me."

He decided to write no more fiction as he had so many other things to do.

On Jan. 4, 1914, thirteen months following the aforementioned letter, Osler received a telegram from Mitchell's son John which read: "Father died this morning." Under it Osler inscribed: "One of my dearest friends. Had I been a son he could not have been kinder to me during the five years of my life in Philadelphia. Professionally and socially he did everything to further my interests though I had no claim upon him other than a mutual interest in scientific medicine and in literature."

Weir Mitchell's claim to greatness in the field of neurology is based on his many brilliant observations backed by accurate physiologic studies. Indeed, his broad knowledge of physiology and his contributions to it have been acclaimed by leaders in that field. His place in neurology is not founded on a single immortal discovery but is rather the result of consistently important controlled work. He would have been a leader at any period. In the period of American neurology in which he worked his leadership carries with it the undisputed title father of American neurology.

Dr. William Francis, librarian in charge of the Osler Memorial Library of McGill University, pointed the way to the Osler-Mitchell correspondence and to many high lights in the latter's life.

Abstracts from Current Literature

THE NEUROLOGY OF HIPPOCRATES. A. SOUQUES, Rev. neurol. **1**:1 (Jan.); 177 (Feb.) 1934.

As a sequel to his brilliant essay on the neurology of Galen (*Rev. neurol.* **1**: 296, 1933; abstr., ARCH. NEUROL. & PSYCHIAT. **31**:845 [April] 1934), Souques has delved into the works of Hippocrates as translated by Littré. The vast wealth of information contained in the ten volumes of text, translation and annotation that required twenty-three years of work on the part of Littré has left unrecognized certain features that Souques brings out with penetrating insight. This applies particularly to the vivid description of tuberculous spondylitis with its accompanying nervous disorders and also to that of postdiphtheritic paralysis, which is usually credited to Aretatus seven centuries later.

"Life is short and art long, the occasion fleeting, experience deceiving and judgment difficult." This is the famous first aphorism of Hippocrates, and it has been handed down in cameo-like perfection throughout the ages. Yet in 1804 Boulet even denied the existence of Hippocrates. While the life of the "divine old man" is full of uncertainty and many legends have had to be discarded, Hippocrates was undoubtedly celebrated during his life and is mentioned by ten different contemporaries, including Plato, Ctesias, Aristotle and others. Hippocrates was born about 460 B. C. at Cos in the Aegean archipelago, at the time of Pericles. He belonged to the Asclepiad family, being a descendant on his father's side from Asclepias. In this family the father passed his knowledge on to his sons. This was customary in those days, although an outsider might attach himself to a temple where the art was practiced.

Hippocrates was educated first by his father Heraclides and later by Herodicus; he learned astronomy, mathematics and literature and especially philosophy from other teachers. It was the common practice in those days to receive solid literary and philosophic instruction. Nevertheless, this education did not prevent Hippocrates from separating medicine from philosophy, and it helped him to found the former on factual observations first and on reasoning afterward. On attaining his majority, Hippocrates wandered from city to city and into far countries, according to the custom of the time, going as far as Egypt and Scythia. In Scythia he observed a peculiar condition in which men lost their potency and became effeminate. Hippocrates discussed this at considerable length, blaming it on the constant equitation. Later commentators have added volumes on this subject. The condition had already been observed in Scythia by Herodicus and was described by Reineggs and by Klaproth about the beginning of the nineteenth century. By this time, however, the men had lost the tendency to clothe themselves as women. The nature of this malady is not yet understood, although apparently it did not consist of eunuchism or anandria and probably not even of homosexuality. On account of the relative incurability, some lesion of the spinal cord or of its roots seems probable. Hippocrates finished his peregrinations and died at an advanced age in Thessaly. In the first century A. D., according to Soranus, his tomb near Larissa was invaded each year by a swarm of bees, whcih deposited a miraculous honey for the cure of aphthae in infants.

There is no authentic portrait of Hippocrates, but his qualities can easily be recognized from his writings. That he had a high conception of medicine, of its dignity and of its duty toward sick people is quite clear, and equally clear is his horror of cupidity and charlatanism. "To become a physician," he said, "there must be natural talents, good education and good habits; one must undertake the study at an early age and must have the love of work and the time for it." Many similar quotations are to be found in the works of Hippocrates.

WORKS OF HIPPOCRATES OR HIPPOCRATIC COLLECTION

Hippocrates is called the "father of medicine," but this he certainly was not, for medicine existed at least in the time of Homer. The blind bard mentioned one hundred and forty-five different wounds and their effects as well as one hundred and fifty anatomic terms, and he had a high regard for the powers of the physician. Moreover, Hippocrates himself stated: "Medicine is not a new science," and the doctrines of Pythagoras, Alcmaeon and Empedocles were starting points for many of his own observations. Even the nomenclature of diseases is mentioned in the works of Herodotus. While nothing is known of the post-Homeric period of five centuries, Hippocrates can still be considered only as a follower, though a follower of genius, and while the surname "father of medicine" is inexact chronologically, it is defensible scientifically.

The works published under the name of "Works of Hippocrates" are not all the product of a single mind; some probably were written earlier and some obviously later than the time of Hippocrates. Aristotle, for instance, stated that "Nature of Man" was written by Polybes, Hippocrates' son-in-law. Littré was the most conservative in picking out certain books which are charactertized by the coherence and clarity of ideas and the concise style that seem to be characteristic of the master. The Hippocratic Collection was formed about three hundred years before the Christian era, and since its entry into the Alexandrian library its content has remained practically unchanged. Nevertheless, during the century or more before the collection was made most of the Hippocratic books had disappeared. The preservation of this collection is due to the interest of the Ptolemies. In regard to these works, Littré stated: "The collection of the Hippocratic books is a disconnected compilation in which it is difficult to find oneself. Different doctrines, incomplete works, mutilated treatises, books that are merely extracts of other books, notes without conclusions, repetitions and finally a disorder that seems inextricable and which truly renders a consecutive reading impossible." Nevertheless, while the books were evidently written by no one man, they all belong to the same epoch and the same school. Souques has gone through this collection with a view to finding neurologic concepts and has found some that seem to have passed unrecognized.

ANATOMIC CONSIDERATIONS

In the time of Hippocrates there was no separation of anatomy and physiology, the single term Φύσις (nature) being used. Dissection of the human body was forbidden, and Aristotle had stated that the human constitution could not be judged from its resemblance to that of animals; nevertheless, in the treatise on articulations there is a fine description of the vertebral column and of the spinal meninges. It is possible, according to Galen, that dissection of animals was not described because in the Asclepiad family it was a juvenile discipline as common as reading and writing. Injuries evidently gave opportunity for topographic study.

The followers of Hippocrates knew nothing of the nerves as such, applying the word νευρὰ also to tendons, ligaments and all white parts of the organism. However, certain white lines in the pale areas called Τόνοι appeared to correspond with the nerves. In the second book of "Epidemics" here is a defective description of what are evidently the pneumogastric and sympathetic nerves. The only difference between the spinal cord and the bone marrow recognized by the followers of Hippocrates appears to have been the presence of membranes enveloping the former. They affirmed that the spinal cord was connected with the brain. Two cerebral meninges were also recognized—a dense one more or less adherent to the cranial bones and a thin one touching the brain. A century later Herophilus coined the names dura mater and pia mater. One of the major errors was the theory that the veins alone contained blood and the arteries contained only air. Hippocrates recognized the pulse beat in the arteries, but he made no contribution to sphygmology. The theories as to the distribution of the veins varied greatly in different treatises; in some it was claimed that they started in the head, and in others, in the liver. Wherever the veins were said to originate, they were regarded as having neither beginning nor end, but it is highly improbable that the Greeks had any notion of the

circulation of the blood, since on the one hand they omitted any mention of the arteries and, on the other hand, they described the veins so erroneously. Even Erasistratus, although recognizing their connection with the heart, separated the ventricles into a sanguineous one (right) and a pneumatic one (left).

PHYSIOLOGIC CONSIDERATIONS

The followers of Hippocrates knew nothing of physiology, interpreting symptoms of disease as due to perversions of normal functions but giving free rein to strange theories, at times ingenious and even profound. Their ignorance of the nerves rendered incomprehensible the functions of the nervous system, such as movement and sensation, as well as that of the vegetative life. Their knowledge of the neurology was apparently limited to a study of the cerebral functions. The brain they considered to be a gland excreting superfluous fluids or distributing them to various parts of the body. Retention of fluids in the brain was said to be followed by apoplexy, epilepsy, delirium, etc. If the fluids were sent to special parts of the organism they were said to produce catarrh and flux. On the other hand, the brain was also considered the organ of intelligence and of sensation. It was regarded as the interpreter of the effects produced by air, and it was believed that that air gave it intelligence. The eyes, ears, tongue, hands and feet were believed to operate according to whether the brain had knowledge, and all parts of the body participated in intelligence in proportion to which they received air; the head, taking in air, was therefore best endowed. When changes in the qualities of air took place, the brain received the impression of those changes. However, the author of "Winds" believed that the blood was the most important factor affecting the intellect. As long as blood retained its constitution, intelligence remained intact, but when it became altered, intelligence failed. Hippocrates and his disciples considered the brain as the organ of thought, while most of his contemporaries placed this function in the heart or even in the diaphragm. Hippocrates mentioned that injuries to the head cause motor and sensory disorders. A distinguished writer said: "It is to be emphasized that, on the one hand, pleasure, joy, laughter and play and, on the other hand, worry, discomfort, discontent and suffering come to us only from the brain. It is through it that we think, understand, see and hear and that we recognize the ugly and the beautiful, the bad and the good, the agreeable and the disagreeable. . . . It is also through the brain that we are crazy or delirious and let fears and terrors assail us either during night or day, with dreams, unreasonable fears, ignorance of the present, strangeness and inexperience. All this we experience through the brain when it is unhealthy, when it is too hot, too cold, too moist or too dry, or when it has suffered some lesion to which it is not accustomed. Madness comes from its humidity; thus, becoming too moist, it necessarily moves and, when it moves, neither sight nor hearing is certain; the tongue expresses that which the brain sees and hears. But while the brain is at rest man is conscious."

The aforementioned work refers to the brain as the organ of dreams. The dreams are considered to be of two types: those sent by divine will and those arising from the condition of the body. Sleep was also considered a function of the brain which the author of "Winds" regarded as being due to congestion and cooling of the blood. Alcmaeon, on the contrary, explained sleep by a reflux of blood from the brain into the veins, that is to say, by anemia of the brain. Although the followers of Hippocrates did not know of the nerves, they considered the brain as the seat of general and of special sensibility. According to them vision was due to the reflexion on the brain of the image formed on the pupil. A vein originating in the membrane of the brain passed to each eye through the skull. The clarity of the pupil and the dark tunics of the eye with the glutinous fluid were recognized. Alcmaeon considered three features in vision: external light, the internal fire of the eye and the intra-ocular fluid that received and transmitted the image. He also recognized the optic nerve. Hearing was said to be due to the striking of sounds against solid bones at the bottom of which was a thin, dry membrane.

The brain could not resound because of its moisture, but it was the brain that heard. The sense of smell was regarded as being due to odors that reached the brain directly through the nose and that were not stopped by any bony barrier.

CLINICAL CONSIDERATIONS

While Hippocrates' knowledge of anatomy was superficial and his explanation of physiology was imaginary, his clinical sense was profound and real. Hippocrates knew how to observe, and by collecting facts and comparing them one can draw up a morbid syndrome. On the other hand, to interpret facts, a knowledge of anatomy and especially of physiology is necessary, and he did not possess that knowledge. It followed, then, that his clinical descriptions have not been outgrown although his interpretations have today fallen into complete discard. The humoral theory of disease, however, was undisputed until the nineteenth century and appears to be coming into its own again.

I have not encountered in the "collection" any document which can with certainty be considered to deal with neuritis or neuralgia. In speaking of diseases of the hip he noted pain posteriorly running down the lower limb; the pain was of long duration, but not fatal. In the opinion of Souques, the disease referred to was not coxitis but sciatic neuritis. Hippocrates practiced cauterization over the painful points. He also mentioned paralyses of the lower limbs following the eating of vegetables, but there is not enough information to make certain of the nature of the disturbance. In his treatise on the joints he separated the traumatic from the spontaneous form of disease and noted the gibbus and the compression of the spinal cord with severe "stupor" of the lower parts. The lower limbs were chilled, and the urine and feces were suppressed. It was customary to treat these subluxations by strapping the patient to a ladder, with the head down and allowing the ladder to fall a certain distance. He stated that when the curvature occurred above the diaphragm in cases of spontaneous subluxations there were often firm tubercles in the lungs. Moreover, in the words of one of the aphorisms: "Those who become hunchback as a result of asthma or cough, before puberty, perish." The treatise goes on to state that in persons affected by curvature below the diaphragm, lesions of the kidneys or bladder were found, and there were apt to be abscesses in the lumbar and the inguinal region of long duration that were difficult to cure. Moreover, in such cases the spine was longer, but there was less tendency for hair to grow on the chin and pubis and less sexual activity than in persons with a curvature above the diaphragm. Hippocrates believed that those who sustained spinal curvature in the adult period of life, especially if they became fat, survived, but that few lived beyond the age of 60. In the book on "Internal Diseases" there is a statement concerning drying up of the spinal cord, which Hippocrates attributed to venereal excess. The condition was characterized by generalized pains so intense that sometimes the lower limbs could not be flexed; there were constipation and dysuria; swelling of the limbs occurred and ulcerations appeared over the buttocks; the malady was difficult to cure, even by cauterization. Nothing else in the books, however, indicates the presence of syphilis in Greece at this time. In the treatise on "Articulations," Hippocrates described many trophic disturbances due to unreduced dislocations; he noted the failure of the dislocated arm to grow and the wasting of the point of the shoulder. The atrophy of the proximal portions was accompanied by changes in the forearm and the hand. A similar picture was painted for unreduced subluxation of the hip. Hippocrates also noted muscular atrophy following fractures and attributed it to compression by bandages. To cure this he frequently applied compression above the location of the atrophy and employed bathing and massage.

In the second book of the "Epidemics" there is a note which seems particularly significant. It concerns spontaneous luxation of the cervical vertebrae and the consequent paralyses. It seems to deal with possible diphtheritic paralysis rather than with subluxation, since the paralysis was noted as a complication of angina with aching of the neck, swelling below the mandible, return of liquids through

the nose, nasal speech, difficult swallowing and no direct suffocation. The uvula was atrophied; the paralysis occasionally affected the face and the palate as well. However, the paralysis did not extend to the whole body, seldom reaching beyond the arms. The patients spit up "cooked material" and suffered from shortness of breath. Those with fever suffered from marked dyspnea, drooling of saliva and swelling of the veins. All had cold feet, but especially those with fever could not stand up. Why this condition was considered due to spontaneous dislocation of the neck is not altogether clear, but it may have been due to concurrent paralysis of the neck. This opinion was commonly held at the time of Hippocrates, however.

In the chapter concerning dentition there are thirty-two propositions, of which twelve resemble a litany and may be reduced to the following: Ulcers of the tonsils appear in two forms. The first type remains stationary; the other forms rapidly, recurs with a presentation of the same symptoms, eats into the tissues, extends to the palate and pharynx and then forms serious ulcers. The first form is benign; the second, malignant. In some instances the ulcers produce concretions resembling spider-webs; in others they are accompanied by the coughing up of phlegm and of cooked material and by disorders in swallowing, speaking and respiration, by cough and by pain. This outline antedates by seven centuries the description of Aretaeus, who is generally given credit for describing diphtheria. Hippocrates mentioned as particularly dangerous the inflammations in which there was no manifest lesion of the throat or neck but which caused pain and dyspnea and suffocated the patient on the same day or on the second, third or fourth day—a description suggesting laryngotracheal diphtheria. That the followers of Hippocrates, who possessed the rudiments of anatomy, should attribute diphtheric paralysis to spontaneous luxation of the cervical vertebrae is conceivable, but that Littré should adopt and defend that thesis is somewhat of a mystery since he was well grounded in the knowledge of anatomy and pathology. Postdiphtheritic paralysis was again brought to the attention of the world about twenty years before the translation of Littré by Břetonneau, although isolated observations had been made previously. It is apparent that Littré was not familiar with these works.

The various types of delirium, headache and vertigo are described in considerable detail with the beneficial effect of venesection, purgation and even trephination. In the seventh book of the "Epidemics" there is a perfect description of ophthalmic migraine: "In the case of Phoenix there was a light resembling a flash of lightning, usually before the right eye; after a short time there supervened a violent pain in the right temple, then in all the head and in the neck to the place where the head is attached in the posterior region of the vertebrae; also if he was forced to move the head or open the mouth he suffered from a hard spasm. Vomiting, when he could bring it about, stopped the pains or relieved them. He was also relieved by bleeding. Hellebore produced evacuation of all sorts of material."

In discussing wounds of the head, Hippocrates gave excellent pictures of meningitis, both posttraumatic and otitic. The convulsions occurring on the contralateral side were particularly emphasized as well as the high fatality in general resulting from wounds of the head. Moreover, fever, delirium, vomiting, hemiplegia, monoplegia and sharp cries were noted as other phenomena resulting from injuries of the head. Hippocrates even described late posttraumatic cerebral hemorrhage and gave an excellent report of a case of meningitis following an old suppuration of an ear. In the little work on vision the following lines occur: "When sight is lost without apparent disease of the eyes, an incision must be made in the parietal region, the soft tissues dissected, the bone trephined and the enclosed fluid evacuated. That is the proper treatment and in this way the patients recover." There is little doubt that Hippocrates recognized amaurosis due to choked disk.

In scattered parts of the "collection" there are references applicable to cerebral apoplexy with its problems, its onset with ringing in the ears without fever, vertigo, slowing of speech and paresthesias. "The subject in full health is taken with a sudden apoplexy; he immediately loses power of speech and of movement; he puffs with his mouth half open; if he is called or moved he only groans but under-

stands nothing; he secretes urine in large quantities involuntarily. If fever does not arise he dies in seven days; if it does arise he usually recovers." Fever, therefore, was thought to play a large rôle, in the prognosis, and in several other places in the text various other phenomena of apoplexy are detailed. In contrast to the excellent clinical description, the pathogenesis leaves much to be desired. Apoplexy was considered to be due to age, to cold, to excesses in drinking; it was explained by retention of impure bile or phlegm, by acrid fluxes which fill up the brain, chill and vitiate the blood of the veins. The treatment for common apoplexy was bleeding, bathing the patient with warm water and purgation, but the grave prognosis was always recognized.

The followers of Hippocrates described epilepsy in detail from the clinical standpoint and raised objection to the consideration of the disease as something divine. They took issue with the charlatans and imposters who laid claims to curing the disease. "The subject loses consciousness and the power of speech; he stifles, foam runs from his mouth, he grinds his teeth, his hands are clenched, his eyes diverge and sometimes the excrements escape. The spasms occur sometimes on the right, sometimes on the left, sometimes on both sides of the body . . . . the whole body is drawn in all directions; the different parts contract and the patients are without feeling, deaf to what is said, blind to what is seen, insensible to pain. . . . Patients with disease of some duration know when they are about to have an attack; they flee and hide themselves in their home if it is close; if not, in a solitary location where their fall will have fewer witnesses, and lie down immediately." Hippocrates described repeated attacks of status epilepticus in case reports, and he noted the beneficial influence of fever on epilepsy. The etiology was based on heredity, yet it was thought that the child of an epileptic person could be healthy because of purgation of the brain before birth. It was stated that most of the young infants who were subject to epilepsy died, but that those who survived retained the signs of the disease in the deviations of the mouth, the eye, the neck or one hand. Hippocrates emphasized the effect of hot weather on these infants and noted the baneful effect on the intelligence and activity. This grave outlook is not altogether borne out by modern studies. In the fifth section one reads: "Epilepsy which begins before puberty can be cured, but that which comes on at 25 years ordinarily does not end except with life." Further, it was stated that persons who had the disease usually died, but if not, they recovered rapidly and spontaneously, and the physician could not be of much assistance. Epilepsy due to arrested menstruation, the convulsions of dentition and the climatologic effects on convulsions are noted in other passages. The concept of water on the brain as a cause of epilepsy was probably derived from the examination of epileptic goats who had hydatid cysts in the brain. Seizures limited to the side opposite the injuries to the head and their treatment by trephination formed part of the Hippocratic doctrine; for epilepsy of spontaneous origin the treatment was by hygiene and regimen. "Whoever knows how to produce in man such a change, notably by regimen is also capable of curing this disease, provided he can recognize the fitness of proper means without purification and magic artifices and all this charlatanism."

Tetanus, occurring after wounds of every type in all parts of the body or after burns or compound fractures and sometimes in the absence of visible injury, was well known to Hippocrates. In the seventh book of the "Epidemics" the following statement appears: "The captain of a large ship suffered crushing of the index finger and lower bone of the right hand by the anchor; inflammation, sloughing and fever followed. Later he complained of his tongue, saying he could not speak. His jaws locked, and then the neck was involved. Three days later the patient was in opisthotonos, and on the sixth day he died." Several clinical pictures were given, and at least three different forms of tetanus were recognized. Tetanus was treated by steam baths, application of lotions, hot ointments, fumigations and even bleeding.

Rabies in animals was probably known to Homer, yet there has been some question as to whether man could be affected. Aristotle claimed that man was not susceptible. Aretaeus claimed that rabies could develop in man as a result

of inhaling the breath of a rabid dog and without sustaining a bite. It is probable that Hippocrates knew of its occurrence; however, the only passage dealing with this is brief and unclear: "Phrenetics drink little, are disturbed by noise and have tremors or spasms." Polybus spoke of the *pheugydros* (persons with hydrophobia) who feared water and died rapidly.

It is possible that alcoholism was less frequent and less severe in hippocratic times than at present, but simple intoxication is mentioned. "Timocrates drank much. After being seized with mania, due to the effect of black bile, he took remedial purges; the evacuations were abundant . . . . he slept; the slumber lasted all night, even till the sun was high on the horizon. During sleep it seemed to his attendants that he did not breathe and he appeared dead and he perceived neither act nor speech. . . . The patient lived and awoke." In other instances the comatose states may have been due to something more than pure alcoholism, and Souques expressed the belief that alcoholic coma was confused with cerebral apoplexy preceded by intoxication. Hippocrates described alcoholic delirium as follows: "The liver swells and presses against the diaphragm; the patient becomes delirious. It seems to him that there appear before his eyes snakes and other animals of all species, goblins that are fighting, with himself in the midst of the combat; and he speaks as though seeing fights and wars; when he dozes he jumps from his sleep and is afraid, seeing frightful things. . . . . when the delirium ceases he comes to his reason and replies normally, knowing everything he says. Then suddenly again he is under the same spell." The trembling of the hands in the delirium was noted. Drunkenness was treated by emetics, hot lotions and bleeding and, curiously enough, by pure wine. The statement "it is good to vomit after drunkenness" is found in the third book on Regimen.

Hysteria or uterine suffocation is described in terms that make it difficult to classify; some symptoms resemble those of present-day hysteria; most of them certainly do not. Migrations of the uterus were blamed, and the clinical aspects were said to vary according to the position taken by the uterus. The uterus was said to wander not only throughout the abdomen but up into the head and down as far as the feet, producing spasms, pain, suffocation, strangury, convulsions and tumors. To distinguish hysteria from epilepsy, pressure was applied with the fingers; if this was felt the attack was hysterical; if not, the attack was epileptic. Hippocrates recommended treating women with hysteria by marriage and pregnancy and the attacks by strong tastes, odors, purges and pessaries.

While less is said about mental disorders, the author of the second book on "Prorrhetics" recognized the hereditary predisposition and the existence of recurring or periodic psychoses. The manic excitation of toxic-infectious states, the violent delirium with headache and the vomiting and insomnia, most likely due to acute febrile diseases, probably do not represent true mental disease, but in the book on the "Glands" it is stated that when the flux turns excessively toward the brain the intelligence is disordered; the patient comes and goes thinking and seeing something else than reality and portraying the character of the disease in mocking smiles and strange visions. Moreover, Hippocrates described depressed states with disgust of life and ideas of suicide in striking terms and recommended treatment by mandrake root in a smaller dose than that necessary to cause delirium. Happy deliriums were considered less dangerous than sad ones. The interchange of depression and epilepsy is spoken of, but it seems probable that epileptic deterioration is here in question. The healing effect of the appearance of hemorrhoids was attributed more to the metastasis than to the bleeding. The theory of fluxes, deposits and metastases played a large part in ancient medicine, but it may have contained a morsel of truth, appearing today as the fixation abscess. Neurasthenia, psychasthenia, hypochondria, obsessions, phobias, etc., were observed by hippocratic physicians, and the difficulty in their management was noted. "Worry is a difficult malady. The patient seems to have in his organs a thorn that pricks him, anxiety torments him, he flees the light and men, he loves the shades, he is a prey to fear, he is harmed by contact and he has disturbed visions and frightful dreams." The depressed state was often associated with

digestive troubles: "The patient is equally uncomfortable fasting or full; when he is empty his bowels rumble, he suffers with pain over the heart and he vomits various materials from time to time; if he has eaten he suffers flatulence. The head is painful, the whole body suffers pins and needles, sometimes in one place, sometimes in another. The disease lasts long and subsides slowly if it ever does." Phthisis dorsalis was thought to be due to a flux running through the back. The loins were painful, and the head was empty. "It attacks principally young married people and people given to sexual excesses. They have no fever and a good appetite but they grow thin. If you ask them they reply that numb sensations seem to run from the head down the spine; after urination or defecation there is a flow of sperm, they lose potency, they suffer nocturnal pollutions whether or not they lie with a woman . . . the head is heavy, the ears ring." Nicanor was obsessed with sounds of the flute; at the first notes terror possessed him. He said that he could hardly contain himself when it was night, although if it were day he could listen to the instrument without experiencing any emotion; and the condition lasted a long time. Democles could not pass close to a cliff or over a bridge, or close to the shallowest pit, but who could walk in the pit with comfort.

GENERAL CONSIDERATIONS

Before closing it will be of interest to survey the general ideas of Hippocrates on the natural history of disease. As regards etiology he stated: "All diseases arise from internal things, such as bile and phlegm, and from external things, such as fatigue, wounds, overheating, chills, excessive drying and excessive moisture." Aside from traumatism, Hippocrates recognized two groups of morbid causes: food and exercise, for the one part, and seasons and climates for the other. Health represented a satisfactory balance of food and exercise. If there was a qualitative or quantitative disturbance in regimen or hygiene, disease followed. Lacking ideas of physiology and chemistry, the nature of these disturbances was naturally vaguely understood. It was well known that food was introduced into the digestive tube and that it was transformed into fat, muscle, bone, etc., but nothing was known of the intermediate stages. Today one recognizes various diseases of metabolism.

Hippocrates emphasized the influence of the seasons and climates. If changes occurred bruskly, diseases proper to each season attacked the susceptible persons. This was the *genius epidemicus* of the ancients, although in their sense the word "epidemic" corresponded to our "seasonal constitution"; if a disease were epidemic, however, the cause was to be found not in the regimen but in the air which was respired, and therefore "one must get away as far as possible from the localities invaded by the malady."

Meteorology and astronomy were seriously studied in relation to disease as indicated in the excellent book "Airs, Waters and Places," and directions were given to the student to pursue his researches accordingly; moreover, the manner of living of the inhabitants was important to know, since the student could predict according to the season which general disease would affect a city in summer or in winter and which persons were particularly liable to be affected; moreover, with this knowledge, a physician would be better able to protect the health of the citizens. Particular circumstances are given, such as the following: In a town exposed to the hot winds of the south "the children are seized with convulsions, with difficulty in respiration, accidents which one would imagine as causes of infants' disease, that is, epilepsy." Hippocrates emphasized the nature of waters, showing which were healthy and which unhealthy. He stated that when the winter was austral, wet and mild and the spring was boreal, cold and dry, residents were subject to paralysis, whereas, if the autumn was rainy and austral, there were, in the following winter, headaches and other grave diseases of the brain. The severe atmospheric changes were particularly to be feared and the rising and setting of certain constellations to be watched with care. At the present time it is impossible to condemn or support these theories, says Souques.

Meteorology has had many advocates in the past, and even now seasonal variations, for example in epilepsy, are recognized but too little studied.

How did Hippocrates interpret the influence of food, exercise, season and climate on health and disease? Health was the resultant of perfect balance of the four humors (blood, phlegm, bile and black bile) and of their corresponding qualities (hot, cold, dry and moist), and if regimen, hygiene and the circumambient medium left the humors intact and well balanced, health was maintained. If one or the other of these factors was disturbed, disease resulted.

Laënnec said: "All the medicine of Hippocrates seems to fall into the following systematic idea: Among the symptoms that a disease presents, there are some that are characteristic of it and there are others that may be found in all diseases." Hippocrates, a semiologist rather than a nosologist, paid attention to the symptoms common to all diseases. He has been reproached for discussing the symptoms proper to each one, for seeing the organism and not the organ, the diseases and not the disease. This reproach, however, is not merited. It holds for the acute febrile conditions, but it must be remembered that in these disorders the whole organism is affected. In reality, Hippocrates also considered the diseases of the separate organs; he recommended careful examination of the diseased organ and then the others, particularly those that are related to the first one. It is true that he did not describe a dozen diseases of the bladder, four types of jaundice, etc., as the Cnidians did, but he reproached them for not paying more attention to prognosis. To Hippocrates, prognosis was of capital importance and differential diagnosis was sacrificed. "The finest physician appears to me to be the one who can foretell the future, declaring to the patient the present, the past, and the future of his disease. Stating that which the patients omit, he will gain their confidence, and, convinced of the superiority of his knowledge, they will not hesitate to put themselves under his care. He will treat the disease all the better for knowing from the present condition how to foretell the future." Elsewhere he expressed himself in these terms: "He who desires to learn how to foretell accurately which patients will not die and which will succumb, which will be sick many days and which just a few should arrive at his judgment by a study of the signs and by comparison of the respective value as described; he must have a deep understanding of the signs and other symptoms and must not forget that in every year and every season the bad signs forecast trouble and the good signs success, because these signs which I have enumerated are verified in Lybia, at Delos and in Scythia." It is unquestionable that certain hippocratic physicians abused prognosis, and "experience is fallacious," as expressed in the first aphorism, is held up as a byword.

The hippocratic doctrine of crises and critical days was connected closely with prognosis. The triple period of the evolution of disease—onset, acme and subsidence—was interpreted in terms of common experience. The expulsion of disease matter occurred by the urine, vomitus, feces, expectoration, sweat, etc. However, the morbific material could be collected in some other point, as in an abscess which would require evacuation.

It has been said repeatedly that Hippocrates remained inactive in the face of a disease and that his therapeusis was only a meditation on death. However, to sustain this statement one could not have read the "Collection." Hippocrates wrote a treatise on medicaments, but this has disappeared. He employed numerous and varied medicines, and his followers abstained only in cases of incurable diseases. He emphasized the necessity for timely action. He believed in the healing power of nature and attempted to use the manifestations in the treatment. If patients got well when they broke into a sweat, for instance, he gave other patients diaphoretics to procure a similar favorable result. On the whole, Hippocrates recommended not only to imitate nature but to do it early and at the right time. Hippocrates counseled one to avoid medicaments only at critical periods. Prevention, hygiene and regimen are frequently alluded to: "I believe firmly that the physician should study human nature and seek carefully, if he wants to practice his art successfully, what relation man has with his food, with

his drink and with his way of living and what influence each exercises on each individual." When it was not possible to prevent, Hippocrates sought to heal and if he could not cure, to solace, because he knew that the comforting of suffering was a divine task.

To sum up, the anatomic knowledge of Hippocrates was rudimentary and his physiologic knowledge was almost nil, but his clinical descriptions were prodigious for his time. In the field of neurology one finds his descriptions of contralateral disturbances in cerebral diseases, of meningitis following trauma or otitis, of the cure of blindness by decompression, of cerebral apoplexy, of generalized and partial epilepsy, of ophthalmic migraine, of diphtheritic paralysis, of tetanus, of alcoholism, of the hereditary predisposition to mental diseases and of the periodicity of certain psychoses, of depressions, obsessions and phobias, of the paraplegias and quadriplegias following compression, contusion or concussion of the spinal cord, of Pott's disease, of reflex amyotrophy and of sciatica. All these subjects constitute original works which in the domain of neurology make Hippocrates a clinician of genius, the greatest of all antiquity.

FREEMAN, Washington, D. C.

HISTOPATHOLOGY OF THE VARIOUS TYPES OF REACTIONS OF THE CENTRAL NERVOUS SYSTEM: AN ANALYSIS OF THE STRUCTURAL CHANGES IN THE PARENCHYMA OF THE CENTRAL NERVOUS SYSTEM. KARL SCHAFFER, Jahrb. f. Psychiat. u. Neurol. **51**:237, 1934.

According to Schaffer there are two important determinants of the histopathologic picture of reactions of the central nervous system; one is the pathogenic factor and the other the morphologic. From the point of view of pathogenesis, the reactions of the central nervous system may be divided into two principal types, the endogenous and the exogenous; the respective histopathologic pictures of these two types are definite and can be sharply distinguished from each other. Neoplastic formation represents a different type of reaction, discussion of which the author does not include in this contribution.

In studying the changes due to endogenous or to exogenous changes, one must take into consideration the structural elements in which the reactions take place, i. e., the ectodermal and the mesodermal elements. The ectodermal elements consist of neuronal and neuroglial components. The neuronal elements form systems—conduction apparatuses having a common neurocellular origin, a more or less "closed" course in the form of systems or tracts and finally a common end-station. These systems represent the anatomicofunctional structural units of the central nervous system; they are of two kinds, the long and the short; the former are known as the central long tracts; they are: (1) the centrosegmental, (2) the systemic and (3) the germinal plate structural units of the central nervous system: It must also be borne in mind that the cellular origin of such a system represents not only its anatomicofunctional center but also its trophic center, so that whenever that center becomes diseased by endogenous or exogenous noxae the tract originating from that center becomes degenerated.

There are two principal types of neuroglial structural elements, the ventricular and the paraventricular glia. The former is the ependyma; the latter, the dendroglia of the nerve parenchyma from which there are derived astrocytes and oligodendroglia. In connection with the neuroglia it must be borne in mind that the mesoglia or Hortega's microglia—an element which has its derivation from the vascular system—is not ectodermal but mesodermal. The ectodermal dendroglia supports and provides nutrition for the neuro-ectodermal elements, whereas the oligodendroglia, like the mesodermal microglia, plays an important rôle in the process of removing the products of disintegration.

Morphologically, parenchymatous changes of the central nervous system are divided into diffuse, disseminated and multiple and circumscribed topicolocal reactions limited to definite systems.

In order to appreciate the biologic value of a pathologic process an investigation of the minute morphologic details making up the formal characteristic of the process is insufficient without a study of the genetic characteristics which eventually give insight into the causation of the changes. It is therefore essential first to determine with modern histotechnical methods the substratum of the morphologic changes, and having accomplished this to assort the changes according to the type of the structures affected. After this, it must be ascertained which determinant typologic change is primary and which is secondary.

In studying the problem in this manner it will be found that the pathogenesis is the controlling factor, because its nature, whether endogenous or exogenous, determines the type of reaction of the central nervous system.

A. Reaction Types Based on Endogenous Factors.—Under the designation of "endogeny," Schaffer has in mind genuine neuro-endogeny in its narrow sense, i. e., that the primary disease is in the central nervous system itself which is poorly developed ab initio and predisposed to disease. In contradistinction to this there also exists a "somato-endogeny": pathologic changes in the body, such as a primary disease of the liver or of the reticulo-endothelial system, which may lead to secondary changes in the central nervous system, so that as far as the central nervous system is concerned somato-endogeny represents a reaction due to exogenous noxa.

Reaction types of the central nervous system in neuro-endogeny: On an idiotypic basis, i. e., in pathologic heredity, there exist two types of disease of the neuro-ectodermal tissue: either neuronal alone, a heredodegeneratio neuronalis, or neuroglial alone, a heredodegeneratio neurogliosa. Each of these types represents a primary disease of the respective tissues—an abiotrophy. In their mature state the neuronal elements are stable elements incapable of multiplication; a primary disease in them is manifested only by progressive degeneration. The neuroglial elements, on the other hand, the immanent property of which is multiplication, serve as secondary "filling in" structures when the parenchyma has been injured, but when the dendroglia becomes primarily diseased and begins to proliferate it does not replace the neuronal elements but destroys them by compression.

An exclusively primary disease of the neuronal elements represents a neuronal electivity manifested by a primary disease of the ganglion cells. This type of disease is not to be confused with primary degeneration of the nervous system previously described by Schmauss, in which certain poisons produce a primary and elective fiber disease of certain systems; Nonne and Fründt, and later Schimazono, have shown that in these conditions there occurs local and bilateral disease along the course of the vessels which may give rise to pseudosystemic combined column degeneration.

Endogenous neuronal disease may occur in two principal forms: (1) systemic degeneration (systemic neuronal electivity) in which the cells of origin of definite neuronal systems degenerate progressively, followed by a degeneration of the affected system; (2) ubiquitous neuronal electivity in which the degeneration is not limited to system centers but affects all ganglion cells, central, peripheral and vegetative. Examples of systemic neuronal electivity affecting the voluntary motor system are familial spastic spinal paralysis, nuclear bulbar paralysis, nuclear spinal muscular atrophy and amyotrophic lateral sclerosis. Examples of systemic neuronal electivity affecting the extrapyramidal motor system are hereditary chorea and dystonia lordotica; those affecting the spinocerebellar system, Friedreich's disease, and of those affecting the cerebellum alone, Marie's cerebellar ataxia. The classic example of ubiquitous neuronal electivity is the Tay-Sachs form of amaurotic family idiocy in which no ganglion cell, from the cortical gray matter to the intramural sympathetic nerve fibers in the intestine, is spared. It is noteworthy that in this disease there is an almost total absence of involvement of the mesoderm of the meninges and vascular apparatus, which is in striking contrast to the severe ubiquitous ectodermoneural disease. It is also noteworthy that in this exquisitely ubiquitous disease of the nerve cells, the neuroglia participates only secondarily by functioning as a scavenger in the removal of the intracellular products of degenera-

tion. The gangliocellular process in this disease represents a fully developed ubiquitous process in the infantile form, which is less marked in the juvenile form and still less in the adult form. The focal as well as the diffuse gangliocellular inferiority is usually associated with evidences of other developmental defects in the central nervous system; the latter may be macroscopic in the form of segmental hypogeneses or microscopic and manifested by abnormalities in the size, shape and position of the ganglion cells.

Endogenous reaction of the neuroglial elements: If one were to postulate the occurrence of a primary elective abiogenesis of the neuroglia—a primary proliferation of the dendroglia—the Krabbe-Scholz form of familial sclerosis would be the best example of such a process. In this disease there occurs progressive glial sclerosis in the cerebral hemispheres, in the centrum semiovale, compressing the nerve fibers coursing through this area and leading to a secondary degeneration of both pyramidal tracts. In a process of this nature it would be improper to speak of a "system disease," because the neuronal systems per se are not primarily affected, so that until the etiology and pathogenesis of such processes have been established the occurrence of an endogenous reaction of the neuroglia must be regarded merely as a hypothesis.

Somato-endogenous reactions: Nerve parenchyma may be affected focally or diffusely by disease originating outside the central nervous system. A good example of a local disease of this type is infantile hepatitis, or hepatic abiotrophy (Kehrer and Miskolczy) beginning during fetal life, whereas Niemann-Pick's disease or splenohepatomegaly is a good example of a diffuse disease. Histopathologically however, these two principal forms of somato-endogenous reaction disclose the ectoderm and the mesoderm affected to the same degree and both of them simultaneously so that the process cannot be regarded an elective one.

B. Reactions of the Central Nervous System to Exogenous Noxae.—Schaffer divides these reactions into two large groups: (1) reactions to infections and (2) reactions to intoxications.

Reactions due to infections: These are divided into those due to visible and those due to invisible noxae. The infections due to visible noxae are best illustrated by syphilis and tuberculosis, which appear in the form of the well known granulomas. Those due to invisible noxae are of special significance because they represent neurotropic reactions which may be manifested in three principal forms: (1) reactions due to noxae affecting systems, such as the poliomyelitides; (2) reactions due to noxae not affecting systems, such as multiple sclerosis; (3) reactions due to noxae producing simple inflammations by traveling along neural channels, such as lyssa and herpes encephalitis. It is noteworthy that the mesodermal character of the inflammatory reaction is common to all three forms of reaction due to invisible noxae, and although neurotropism is also a characteristic feature of all three forms it differs greatly in the various forms. Thus, in the first form the neurotropism is manifested by an anatomic system electivity; in the second the noxa has an affinity for lecithin—a chemical reaction—and in the third there exists a general neural electivity, the noxa utilizing the neural tube as the medium for its propagation.

Reactions due to intoxications: These types of reactions are observed in cases of poisoning due to lead, in B avitaminosis, in cases of beriberi, in cases of poisoning due to epinephrine, to insulin, and to bulbocapnine and in cases of thyrotoxicosis, yellow atrophy of the liver and uremia. Morphologically there is nothing characteristic about the cases in this group; they all represent a mixed nonspecific type of reaction.

KESCHNER, New York.

THE HORMONE OF SEXUAL MATURATION (A PRINCIPLE IN ONIONS AFFECTING SEXUAL MATURATION IN ANIMALS). I. M. PEISSACHOVITSCH, Rev. franç. d'endocrinol. **12**:205, 1934.

The proof offered by Loeve, Lange, Spohr and Dohrn of the existence of certain substances in some vegetations which produce the same effect in the animal

organism as the follicular hormone led Peissachovitsch to investigate the possible presence of such a substance in the onion (Allium cepa). This selection was motivated by the historical legends attributing medicinal properties to this vegetable (the legend being credited to Juvenal, Pliny and Homer and mentioned in the fourth book of Genesis). In order to determine the localization of a hormonal substance, onions in various stages of maturation were used. Through a more or less complicated method of treatment of the vegetable a white or grayish water-soluble sediment was obtained. Experiments with this substance were carried out on castrated and prepubescent female mice, rats and rabbits. The administration of the substance to castrated animals does not cause rut (estrus); it accelerates sexual maturation in prepubescent animals about one hundred hours after the first administration. There are maturation of the follicles, hypertrophy of the vagina, the uterus and the horns, onset of rut (estrus), the formation of corpus luteum and congestion and hemorrhages in the ovaries.

In adult female rabbits the action of the hormonal substance becomes apparent forty-eight hours after the first administration and manifests itself in hyperemia and hypertrophy of the uterus and the horns and in an increase in the size of the follicles and hemorrhages in them. The ovarian hemorrhage is the most characteristic sign of the biologic activity.

The main alterations in the genital tract and in the ovaries depend, according to Peissachovitsch, not only on the amount of the substance administered but also on the method by which it is given. The administration of one dose at one sitting produces a different reaction as compared with that when the same amount is given in fractional doses at certain intervals. While 0.03 units of the hormonal substance injected in a vein of a rabbit produces forty-eight hours later small ecchymoses in the ovaries, it will cause large hemorrhages at the end of the same time if given in fractional doses over a period of two days. One kilogram of fresh onions produces 1,000 mouse units or 20 rabbit units of the substance. The biologic unit is the minimum quantity of the substance which causes the formation of corpus luteum in the mouse and estrus and hemorrhages in the rabbit. Peissachovitsch claims that the reaction to the substance in prepubescent animals is similar to the reaction to the gonadotropic hormones of the anterior lobe of the pituitary gland and resembles partly the phenomena produced by vitamin E. This observation led him to consider the problem of the possible close relationship between the hormonal principle in the onion, the anterior pituitary gonadotropic hormone and vitamin E. The latter substance, as is known, was found by Evans and Bishop in cottonseed oil, corn oil and butter. He invokes the following facts in favor of such a relationship: autolysis of the fetal tissues in pregnant females deprived of vitamin E; disappearance of the reproductive cells in the male deprived of vitamin E; prevention of sterility with the aid of large doses of anterior pituitary hormone (prolan) in animals deprived of vitamin E, and hypertrophy of the uterus and estrus in prepubescent females following intraperitoneal and oral administration of vitamin E. Peissachovitsch thinks, therefore, that the hormonal substance in the onion and vitamin E are identical in their biologic activity; he adds, however, that the identity is not an absolute one since certain reactions produced by the hormonal substance in the onion are not seen under the influence of vitamin E. He agrees with Wolf that vitamin E and the follicular sex hormones are only excitatory physiologic substances.

Peissachovitsch doubts whether the hormonal substance in the onion is identical with prolan, considering the fact that the gonadotropic hormones, prolan A and B, originate in the anterior pituitary, while the former substance is an extract of a ripe plant. There is probably only an identity in a biologic sense between the hormonal substance in the onion and prolan A and B, and between the hormonal substance and vitamin E. He thinks that it will be idle to speculate concerning their chemical identity so long as the chemical structure of prolan, the hormonal substance in the onion and vitamin E remain unknown. He closes the article with the statement that the substance obtained from the onion is a special hormone of a vegetable cell which produces in the animal organism reactions specific to the gonadotropic hormones.

NOTKIN, Poughkeepsie, N. Y.

A Special Form of Familial Multiple Sclerosis, Resembling Friedreich's Ataxia. B. Brouwer, Ztschr. f. d. ges. Neurol. u. Psychiat. **148**:321 (Nov.) 1933.

Brouwer reports the cases of two sisters with a characteristic picture of Friedreich's ataxia clinically; however, pathologic examination showed a number of disseminated plaques. The patients' father was addicted to the use of alcohol, and their mother suffered from hysteria. One brother and one sister died in infancy; both were idiots. Two other brothers and one sister were well. The disease began in both patients at 8 years of age, with disturbances in gait and tremors of the trunk and the extremities. The oldest sister had severe ataxia and tremors of the head and trunk; there was also ataxia of the legs. Sensation was not disturbed. The ocular fundi showed no atrophy. The upper abdominal reflexes were weak, and the lower abdominal reflexes were absent; there was a Babinski sign bilaterally. A diagnosis of Friedreich's disease was made. In the following years the ataxic disturbances increased markedly, and speech became much worse. Vision became worse because of atrophy of the optic nerves; nystagmus developed. The tongue was slightly atrophic, and the lower part of the right side of the face was slightly weak; swallowing was affected; hearing became impaired on the right; vertigo developed. The feet showed the characteristics typical of Friedreich's disease; the legs became very weak. All reflexes were lost, and there was a Babinski sign bilaterally. The condition remained constant, without remissions. A mild degree of dementia developed in the last few years of life. The patient died of a "grip" infection.

The younger sister was still alive at the age of 33. Her malady began at the age of 8, with disturbances in gait and tremor of the head. At the first examination there was mainly ataxia of the arms and legs; there was no intention tremor; the feet were in the equinovarus position. The reflexes were absent; the abdominal reflexes could be obtained. There was marked hypotonia of the extremities. At the time the case was reported there was almost complete inability to stand. There was no nystagmus, and speech was slow and monotonous. The legs were ataxic; the arms were dyssynergic. The tendon reflexes were absent, and the abdominal reflexes were decreased on the left. There was no Babinski sign and no sensory or mental disturbances. A diagnosis of Friedreich's ataxia was made. Later, mild atrophy of the optic nerves developed, and sensory signs appeared in the form of bilateral astereognosis and decreased muscle sense in all extremities; mental symptoms developed, with delusion and later deterioration; the ataxia reached a high grade. The disease progressed slowly; the optic nerves atrophied; horizontal nystagmus and ptosis developed; sense of vibration was lost in the legs. Serologic tests gave negative results.

Histologic study of the nervous system in the first case showed degeneration of the posterior columns and roots and the pyramidal tracts in the sacral part of the cord. At another sacral level there was a sclerotic plaque in the left anterior horn. In the lumbar and thoracic regions there was posterolateral sclerosis, the disease of the posterior columns spreading over to involve the posterior horns. The axis-cylinders remained intact. In the cervical region there were sclerosis of the posterior columns and circumscribed sclerotic patches. There were sclerotic plaques in the medulla, the nuclei of the posterior column, the left inferior cerebellar peduncle and the tuberculum acusticus, the pyramidal tracts, the reticular substance and the inferior olives. There were sclerotic patches in the cerebellum. Similar plaques were present in the walls of the third ventricle, the left internal capsule, the external geniculate body and the roof of the midbrain. Plaques were found in the cerebrum.

The clinical picture was that of Friedreich's disease; the pathologic changes were those of multiple sclerosis. There was no evidence of congenital syphilis, a similar picture having been described in congenital syphilis by Gianelli. Mondini described a case like Brouwer's. This concerned a woman, aged 32, wth Friedreich's disease, who came of a family with marked mental degeneration. She died at the age of 41. Histologic study showed bilateral degeneration of the spinocerebellar tracts

and slight demyelinization of the pyramidal tracts. There were atrophy and thinning of the cellular layer of the cerebellum. There were, in addition, sclerotic plaques in the cord and brain, with the classic characteristics of multiple sclerosis.

Brouwer believes that his patients suffered from a particular form of multiple sclerosis rather than from a special form of Friederich's ataxia. The occurrence of disease of the pyramidal tract is more common in the former. Cases of the sort described are rare.

ALPERS, Philadelphia.

THE NEGRO AND HIS CHURCH. R. A. BILLINGS, Psychoanalyt. Rev. **21**:425 (Oct.) 1934.

Billings challenges the presumed truthfulness of the often repeated statement that Negroes are inherently religious and says that a closer study of the problem suggests that much of the religiosity has developed as an adaptive reaction to definite environmental situations.

The religious divisions within the race are effected mainly on the basis of the degree of color, but the particular psychic mechanisms are in operation in varied degree in all classes of Negroes, regardless of the shade of color. The groups of Negroes attending the lower class of churches are composed largely of people usually called "blacks." They represent the most unfortunate element of an unfortunate race in that they are very poor and uneducated and are socially ostracized by the white as well as by their own race. Pervading their entire life are feelings of inadequacy, inferiority and deprivation—a source of untold anguish. Much is needed to make up for their deficits in life, and religion and the church provide a seemingly adequate avenue of escape. To make up for lack of amusement, the church provides music of the type found in dance halls. To make up for personal and social limitations, it convinces its followers that they are superior to those about them. To compensate for poverty on earth they are offered rich rewards in the life hereafter, while the devastating waves of hatred are escaped by compensatory professions of great love. The churches, through social sanction, further offer a partial release of some sexual energy.

The church membership in the group comprised under the middle class is recruited from Negroes occupying a higher economic, educational and social level. The pigmentation of the skin is much lighter than in those of the lower class and runs the various shades of "brown." Because of the higher cultural level, these people are more sensitive to social inferiority, but the consciousness of the presence of a still lower group absorbs much of the acuteness and lessens the need for religious compensatory activities, at least in obvious behavior, the compensatory activities being at a more social level, while undischarged emotional tensions are subjected to the process of repression, from which they sometimes escape in the form of peculiar symptomatic behavior.

The upper group comprises persons in the highest economic, social and cultural level within the Negro race. In color, the members belong mainly to the "pale" group. Their churches are often pastored by white ministers, which neutralizes some of the feeling of inferiority as well as satisfying a certain feeling of identity with the white. In general, this group feels itself more kin to the white race than to the colored race. The fact that they find but little satisfying compensation in the presence of darker members of the race, while on the other hand they are prevented by social dictum from passing the white line, makes the "color complex" in this group more acute than in any other group. The bitterness of the situation makes it necessary to seek relief. The church looms as the most feasible surcease, for here they are able to mingle and enjoy the company of fellow sufferers.

While it is true that the fundamental reasons for the different groups of Negroes being found in churches are the same, there are certain factors which have worked to effect a definite division of the membership of the Negro church into three reasonably distinct groups or classes on the basis of color, education and economic and social state, but mainly on the basis of color. It is no great problem why these groups should be found in different churches. Escape, compensation and

repression are the factors that run throughout all of the classes. The fact that each class is different in its life status made it necessary to develop an entirely different form of adaptation. The Negro will continue to take his church seriously just as long as he is handicapped economically, socially and psychically. When these handicaps have been removed there will be a great reduction in the membership of the Negro church, because the purpose it has served and the psychic function it has performed will no longer be necessary.

KARPMAN, Washington, D. C.

LIPOPHAGIC SUBCUTANEOUS DIFFUSE GRANULOMATOSIS: A SCLERODERMIC CONDITION. UMBERTO POPPI, Jahrb. f. Psychiat. u. Neurol. **51**:191, 1934.

In the case of a girl aged 13 years, there developed, within three months, an extensive scleroderma which was most marked over the trunk and proximal portions of the limbs and spared only the palms, the soles, the pubes and the visible mucous membranes. During the first two weeks after the onset the patient appeared to have slight fever. Biopsy of pieces of skin and muscles disclosed: proliferation of the subcutaneous fat, especially of the uppermost layers; permeation of the muscle with numerous globules of fat; the presence in the deeper layers of the subcutaneous tissue of areas in which the fat had entirely disappeared and other areas in which it was partly converted into fatty acids and glycerin and still other areas in which there was normal fat; failure to spare the muscle tissue by the proliferating process, which was especially intense in the layers nearest to the subcutaneous tissue; accumulation of the proliferating elements around the blood vessels, with no tendency to invade them; poorly stained individual muscle bundles, with indistinct and altered striations; areas remote from the subcutaneous connective tissue in which the proliferations had more of an interstitial character and striking fatty infiltrations between the muscle fibers. The blood vessels in the skin and subcutaneous tissue were almost all surrounded and infiltrated by the proliferating elements; their lumens were often narrowed and in some areas even obstructed by swelling and increase of the endothelium. Here and there the nerves were also surrounded by the newly formed elements. The proliferating cells were of the nature of histiocytes, polymorphonuclear eosinophilic leukocytes, a few neutrophils, mononuclear eosinophil cells and plasma cells, a few lymphocytes and an occasional clasmatocyte.

Poppi points out that although it is well known that the anatomic picture in scleroderma may vary in different cases and that there is no parallelism between the damage to the skin and the sclerodermal symptoms and also that the sclerodermal process may affect the viscera and bones in addition to the skin and muscles, he is unaware of any case of this disease in which liponecrosis was a feature in the pathologic process. The term liponecrosis is generally employed to designate a saponification of fats which is associated with a proliferating reaction either of the fat cell itself or of the reticulohistiocytic tissue. In view, however, of the lack of unanimity as to the nature of liponecrosis, Poppi would, for the present at least, apply this term to designate only a destruction of fatty tissue which is primary (mostly due to trauma) and in which the proliferating process is secondary. Classic examples of this form, then, would be liponecrosis of the breast (Brancati and Morone), in which there are collections of liquid fat, and the pseudoscleroderma of the newly born (Diss and Woringer and Constantino); in these cases a lipase derived from traumatized fatty tissue acts as a foreign body which produces reactive processes manifested by the appearance of giant cells. In addition to this form, in which fat necrosis is primary, there may also occur, according to Poppi, other forms in which the fat necrosis is the secondary result of a more or less chronic inflammatory reaction of the reticulohistiocytic tissue; this form he would designate as a "lipophagic granuloma," a term which he believes is applicable to the case under discussion. The unusually large extent of the disease, the histologic features of the tissue reaction and the blood picture (mononucleosis and eosinophilia) are all in favor of an involvement of the reticulohistiocytic system,

although in the present state of knowledge it is impossible to ascertain the determining cause of the disease. The histologic characteristics of the reaction, which is unquestionably inflammatory, do not aid in clarifying the problem.

The pathogenesis of the sclerodermal condition can be readily explained when one admits that it is a disease of the reticulohistiocytic system which has also affected the collagenous tissues of the skin and subcutaneous structures leading to their sclerotization. The occurrence of granulation tissue seems to confirm this theory.

KESCHNER, New York.

THE EGO DISTURBANCES IN THE DREAM LANGUAGE, HYPNAGOGIC HALLUCINATIONS AND SCHIZOPHRENIA. J. KOLLARITS, Arch. f. Psychiat. **101**:19 (Nov.) 1933.

The author describes the results of a series of observations made while in communication with persons in the various stages of sleep and compares these with observations made in cases of schizophrenia and other mental diseases in which language disturbances and hallucinations occur. The summary of his findings is:

1. In conversations carried on with persons who were in a state of sleep of a depth permitting such communication, the following disturbances of language were noted. There was some dysarthria, substitutions of letters, syllables and words, perseverations and inclusion of unnecessary words. The type of production obtained was not altogether identical with the contents of the dreams related by these persons after waking up. To some extent these findings corresponded with those that occur in schizophrenic patients. The most outstanding similarities were the nonsensical nature of some of the sentences, answers that did not seem to be related to the questions and the absence of certain conventional and moral considerations. In some cases it was possible to produce false perceptions through suggestion somewhat similar to what one finds in hypnosis. Mathematical problems were dealt with in a very poor and primitive fashion, showing here as in the conversation in general a tendency to perseverate and to take the easiest way out. Some of the answers seemed to be definitely related to wish fantasies and anticipations in a rather transparent and childlike fashion.

2. The hypnagogic hallucinations were mainly of the optic, and only rarely of the acoustic, type. The latter were particularly frequent if the persons had been carrying on intensive discussions before going to sleep. These hallucinations may contain whole sentences or only parts of sentences, or even parts of words. Their nature is regarded by the person himself as foreign to his ego, the person experiencing a splitting in which he is able to observe his own hallucinations as apart from his ego. Here, as in the language of a sleeping person, one finds such phenomena as word salad, neologisms and broken up sentences which remind one of the language of schizophrenic subjects.

3. The attempt to repeat during the hypnagogic state literary passages or verses learned before going to sleep shows similar disturbances. The repetition suffers from the intrusion of foreign words or even sentences which change the text, sometimes retaining some semblance of form, at others becoming a senseless mixture of words.

4. A similar disturbance was found in the attempt to associate on words given just before the hypnagogic state takes place. One finds there that for a short period the associations are definitely related to the stimulus word. But as the person begins to sink into sleep the associations become less related to the stimulus word, and whether or not they may have any sense in themselves, in most of them no continuous chain of associations could be demonstrated between the stimulus and the words produced.

5. A certain resemblance could be found between these disturbances and the mistakes made in so-called "inner speech" during waking periods. However, the mistakes made in the latter are not as coarse as in the former and show more relationship to the trend in question. With all the similarity that these disturbances have to disturbances in language in schizophrenic subjects, they cannot be regarded

as identical. The schizophrenic person may have a similar disregard for ego direction in his experiences and conversation, but added to this there is a positive dysfunction related to disturbances in will and the delusional systems. The schizophrenic person, furthermore, shows more attempt to relate his fantasy life to what is actually occurring around him. A discussion is taken up of the possible relationships between these disturbances and their possibly physiologic basis, and this is contrasted with what the author considers as the probable organic disturbances in schizophrenia.

MALAMUD, Iowa City.

FRACTURES OF THE SPINE. W. S. HAUGHTON, Brit. M. J. **2**:774 (Oct. 28) 1933.

Crush fractures (compression fractures) of the bodies of the vertebrae may at first present only slight deformity in the roentgenogram, but a crush fracture implies an inflamed bone, and rarefying osteitis soon softens this bone sufficiently to permit gradual or even rapid "wedging" of the bodies if premature weight-bearing is allowed. In regard to treatment, it is important to bear in mind that in most cases of wedge-shaped vertebrae following injury the wedge is shallower in front and deeper posteriorly. Four stages of treatment are described. 1. The patient lies face downward on two tables, placed to form a T, the head and shoulders only resting on the transverse table, the body and legs on the other. 2. The ankles are padded thickly with felt, placed between and around. A rope is made fast around the padded ankles by a "clove hitch," and a suspension tackle is hooked on. 3. The ankles are slowly hoisted from the horizontal to the vertical direction, powerful traction thus being exerted in the axis of the spine and hyperextension in the anatomic sense. This stage should occupy twenty minutes; during it partial or complete reduction of the fracture dislocation should be effected. 4. The table under the body and legs is removed, and on the hyperextended spine a posterior plaster shell, suitably padded with felt (or a complete plaster jacket), is built up and the patient is lowered.

In a usual case, after three or four weeks the patient is placed in an anterior spinal shell by day and a posterior shell by night. After six months, the patient is allowed to become ambulatory in a special spinal support extending from the pelvis to the axilla.

Directions are given for transporting the patient with a spinal fracture. He should be placed face downward on a stretcher, with a roll of coat, blanket or sand-bag transversely under the upper part of the chest and another transversely under the pelvis. The exception is in cases of fracture dislocation of the cervical position of the spine. Haughton suggests that any patient who is conscious but paralyzed in both arms and both legs should be transported on his back, with the head and neck hyperextended over a small hard pillow or sand-bag placed transversely behind the neck and above the shoulders.

FERGUSON, Niagara Falls, N. Y.

SYPHILIS OF THE PITUITARY BODY. FRANK S. KENNEDY and JOHN H. FISHER, Am. J. Syph. & Neurol. **18**:12 (Jan.) 1934.

Gumma of the hypophysis is a rare complication of syphilis. The case here reported was found at routine autopsy on a Negress, aged 58, who had presented no clinical evidence of pituitary disease. The woman had been a patient in a hospital six years prior to death; a diagnosis of pulmonary tuberculosis, heart disease and vascular syphilis had been made. An extensive hemorrhage in the right internal capsule was found—a condition which probably had caused the patient's sudden death. The sella turcica was not distorted, and the pituitary body was of normal size and contour. One third of the anterior lobe, however, was involved in a gummatous process, consisting of numerous miliary gummas. The lesion extended to but did not include the pars intermedia. The pathologic lesion was composed of collections of epithelioid cells, near which were many well formed, large giant cells. In the area involved, nearly all the acinar tissue was

destroyed and replaced by new-formed tissue, which, however, had failed to increase the bulk of the gland.

The literature on the subject of syphilis of the hypophysis is reviewed—apparently completely. Reference is made to thirty-five cases verified by autopsy, fourteen cases verified by clinical findings and thirty-two cases of congenital syphilis of the pituitary body. Most of these were in women, and most showed clinical evidence of pituitary disease—usually diabetes insipidus or dystrophia adiposa genitalis. Positive serologic changes in the spinal fluid were the rule.

DAVIDSON, Newark, N. J.

CARDIAC INNERVATION. J. C. WHITE, W. E. GARREY and J. A. ATKINS, Arch. Surg. **26**:765 (May) 1933.

The relief of cardiac pain and the demonstration of the pathways of cardiac pain impulses have been experimentally approached. A suture inserted around the descending branch of the left coronary artery and brought out through the wall of the chest permitted the temporary occlusion of this vessels in the unanesthetized dog. The resulting ischemia of the cardiac muscle produces characteristic stiffening of the animal's limbs, marked increase in the rate and the depth of respiration and restlessness, which manifestations are believed to be comparable to those produced by angina pectoris in man.

These characteristic behavior changes produced by temporary occlusion of the coronary vessel can be prevented only by bilateral removal of the sympathetic ganglions from the stellate down through the fourth thoracic ganglion or by section of the five upper posterior thoracic nerve roots. They are not prevented by sectioning both vagi, by sectioning the upper intercostal nerves on both sides or by bilateral resection of both stellate ganglia.

Although the relief of four patients with angina pectoris by surgical measures based on these findings proved satisfactory, the authors recommend for routine treatment paravertebral injection of alcohol into the four or five upper thoracic ganglia and their rami. This procedure gave excellent results in 50 per cent of twenty-three patients and failure in 20 per cent.

SPERLING, Philadelphia.

THE MECHANISM OF THE EARLY RELIEF OF PAIN IN PATIENTS WITH ANGINA PECTORIS AND CONGESTIVE FAILURE AFTER TOTAL ABLATION OF THE NORMAL THYROID GLAND. A. A. WEINSTEIN, DAVID DAVIS, D. D. BERLIN and H. L. BLUMGART, Am. J. M. Sc. **187**:753 (June) 1934.

In accordance with clinical studies of the circulation (Blumgart and associates) which formed a rational basis for removal of the normal thyroid gland in cases of congestive failure and angina pectoris, striking relief of pain in the chest has occurred. Observations on the immediate postoperative relief of pain in the chest after total thyroidectomy in nineteen patients are described. The early relief of pain in the chest after complete removal of the thyroid is due to interruption of nerve impulses and is temporary; it occurs immediately after operation and not infrequently reappears before any considerable reduction in the metabolic rate occurs; it is closely analogous to the early effects of cervical sympathectomy. The immediate relief of pain after total thyroidectomy is due to the interruption of afferent nerve impulses from the heart at the time of the operation; permanent relief is related to the lessened work of the heart attendant on the development of the hypothyroid state.

MICHAELS, Boston.

CEREBROSPINAL FLUID SUGAR IN UNCOMPLICATED AND UNTREATED NEUROSYPHILIS. PURCELL G. SCHUBE and ROBERT C. LEWIS, Am. J. Psychiat. **13**:369 (Sept.) 1933.

The amount of sugar in normal cerebrospinal fluid has been variously estimated. The averages usually given fall between 45 and 80 mg. per hundred cubic centimeters; the range, from 40 to 134 mg. Studies of the amount of sugar in syphilitic

spinal fluid have been confusing, some authors reporting increased values, some decreased and some normal. The present study is a statistical analysis of the spinal fluid sugar in 435 cases of untreated and uncomplicated neurosyphilis. In cases of dementia paralytica the range was from 40 to 107 mg.; in cases of tabes without psychosis, from 42 to 112 mg., and in cases of cerebrospinal syphilis without psychosis, from 40 to 86 mg. The means were 63, 64 and 61 mg., respectively. By statistical computation the authors demonstrate no true differentiation of the sugar content, between one type of neurosyphilis and another. There also appears to be no difference between the sugar values in cases of cerebrospinal syphilis and in the normal spinal fluid. DAVIDSON, Newark, N. J.

HEAD INJURIES. S. BERNARD WORTIS and WARREN S. MCCULLOCH, Arch. Surg. **25**:529 (Sept.) 1932.

An experimental study was made of the effects of injury of the brains of cats. Following laceration of various regions of the surface of the brain, the introduction of blood into the subarachnoid space or fracture of the skull there is an increased sensitivity to a standardized convulsant (camphor monobromide). The increased susceptibility can usually be demonstrated four days after the injury and may persist for at least three or four months. Laceration of the brain gives rise to meningocerebral adhesions and a contracting cerebral cicatrix, which causes ventricular distortion. This suggests that surgical measures may mitigate the convulsions in postmeningitic epilepsy, which is refractory to the usual medicinal agents or to encephalography. The introduction of blood into the subarachnoid space did not produce ventricular distortion. Histologic studies showed that lacerations of the brain were associated with destruction of cellular elements, with evidence of glial phagocytosis and glial scarring, and with cerebral deformity. SPERLING, Philadelphia.

THE CEREBROSPINAL FLUID IN MULTIPLE SCLEROSIS. H. HOUSTON MERRITT, Brain **57**:56 (March) 1934.

The findings in 100 cases of multiple sclerosis are reported, and the findings in 968 previously reported cases are summarized. Merritt's own results will alone be abstracted here. The intracranial pressure is usually normal; the average was 131 mm. More than 10 cells per cubic millimeter were found in 18 per cent of 141 specimens of fluid (100 cases). The protein content varied between 13 and 133 mg., with an average of 43 mg., per hundred cubic centimeters. An abnormal gold curve was present in 75 per cent of the cases. Sugar, nonprotein nitrogen, chlorides, sodium, calcium, phosphorus, total solid content and freezing point were nearly always normal. When the cerebrospinal fluid findings are compared with the clinical course (progressive or stationary), a much higher percentage of abnormal conditions is found in the progressive cases. A table gives a summary of the cerebrospinal fluid findings in 1,068 cases of multiple sclerosis that are recorded in the literature. MICHAELS, Boston.

THE PARASAGITTAL GLIOMAS. CLEMENT B. MASSON, Bull. Neurol. Inst. New York **3**:546 (March) 1934.

The author reports four cases of a subcortical growth situated in the mesial surface of the cerebral hemisphere, to which he applies the term parasagittal glioma. The tumor is usually an astrocytoma and produces symptoms and signs which are similar to those caused by a parasagittal meningioma. The outstanding difference in the symptomatology presented by these two tumors are: (1) the prominence of localized or general convulsive seizures as the initial or early symptom in the case of glioma as contrasted with the relatively infrequent and late occurrence of convulsions in cases of meningioma; (2) signs of general increased intracranial pressure are slight or absent in cases of glioma, whereas symptoms of general

pressure are prominent in cases of meningioma. Encephalography was of particular value as a diagnostic measure in the cases reported, and the article contains a number of excellent plates.

KUBITSCHEK, St. Louis.

THE ACTION OF ADRENALIN UPON THE CARDIAC VAGUS. G. STELLA, J. Physiol. **77**:68 (Dec. 19) 1932.

Stella finds that epinephrine injected intravenously into dogs in moderate doses (about from 0.002 to 0.005 mg. per kilogram of body weight), enough to cause increase of arterial pressure and marked slowing of the heart, does not seem to have any direct exciting effect on the cardio-inhibitory centers. Epinephrine administered in these amounts is, nevertheless, not entirely without action on the centers, since it increases the reflex excitability of the cardio-inhibitory centers to afferent impulses from the depressor and the carotid sinus nerves. Bradycardia produced by epinephrine is reflex in origin and due to the arterial pressure acting on the sensitive regions of the carotid sinus and of the territory of distribution of the depressor nerves; its degree, however, is conditioned by a state of increased reflex excitability of the cardiac vagus centers caused by the epinephrine.

ALPERS, Philadelphia.

A NOTE ON THE OCCURRENCE AND SIGNIFICANCE OF AIR IN THE SUBDURAL SPACE AFTER ENCEPHALOGRAPHY. FRITZ CRAMER, Bull. Neurol. Inst. New York **3**:506 (March) 1934.

In the case of a child aged 3 years who was suffering from recurrent convulsive seizures, an encephalogram showed a large quantity of air over the left side of the cortex suggestive of cortical atrophy. Investigation through a trephine opening revealed a large amount of air underneath the dura and outside the arachnoid, in the presence of a normal-appearing cortex. The author suggests the following possible portals of entry to the subdural space: (1) through the arachnoid which ruptured because of distention with air: (2) at the site of injection, and (3) through a previously existing opening in the arachnoid. An unusual accumulation of air over the surface of the brain associated with an absence of cortical markings should lead to the suspicion that much of the air may be in the subdural space and not necessarily indicate cortical atrophy.

KUBITSCHEK, St. Louis.

SPECTROPHOTOMETRIC CHARACTERISTICS OF HEMOGLOBINS. J. H. SHENK, J. L. HALL and H. H. KING, J. Biol. Chem. **105**:741, 1934.

The authors present an optical method for determining in muscle the relative amounts of the two red pigments, muscle and blood hemoglobin. They prepared solutions of muscle hemoglobin free from blood hemoglobin and examined them by the spectrophotometer. Absorption curves were similar to those obtained from blood hemoglobin but were displaced toward the red portion of the spectrum. Spectrographic study showed a marked difference in the ultraviolet absorption spectra of the two hemoglobins and similar difference in the absorption spectra of the globin fractions. Little difference was shown between the acid hematin fractions, indicating that the difference is in the protein part of the molecule. The authors' results also indicate that exercise is a factor influencing the level of muscle hemoglobin.

IRVINE, Boston.

THE DEMONSTRATION OF NORMAL CEREBRAL STRUCTURES BY MEANS OF ENCEPHALOGRAPHY: IV. THE SUBARACHNOID CISTERNS AND THEIR CONTENTS. CORNELIUS G. DYKE and LEO M. DAVIDOFF, Bull. Neurol. Inst. New York **3**:418 (March) 1934.

This article presents one of a series of studies which Dyke and Davidoff have made on normal cerebral structures as revealed by encephalography. Anatomic structures of the various subarachnoid cisterns are reviewed in considerable detail

and demonstrated as they appear in actual specimens and in encephalograms. They have found it possible not only to identify all the cisterns by encephalograms and by stereoscopic examination of the films but to study the actual size, shape and position of these spaces and their relation to adjacent cerebral structures. Numerous plates of encephalograms demonstrating the various structures are included in the article.

KUBITSCHEK, St. Louis.

RESECTION OF SENSORY NERVES OF PERINEUM IN CERTAIN IRRITATIVE CONDITIONS OF THE EXTERNAL GENITALIA. J. R. LEARMONTH, H. MONTGOMERY and V. S. COUNSELLER, Arch. Surg. **26**:50 (Jan.) 1933.

The anatomy of the sensory nerves of the perineum and the operative technic of their resection are described. Resection is suggested for patients suffering from irritative conditions of the vulva, except in the presence of a malignant condition or marked obesity. The authors considered seven cases in which they had operated and seven reported in the literature. There was only one failure; in three cases relief was afforded for over one year, while in the remainder relief from pruritus was obtained, but sufficient time had not elapsed to appraise the results further. The operation, when carefully performed, does not interfere with either the rectal or the vesical function.

SPERLING, Philadelphia.

A CURIOUS FORM OF COCAINE POISONING. F. J. COLLET, Rev. d'oto-neuro-opht. **12**:281 (April) 1934.

A girl, aged 7 years, manifestly degenerated (difficulties of speech, strabismus and facial asymmetry), following the packing of the nose with 10 per cent solution of cocaine exhibited atypical signs of poisoning. There was no pallor or weakness of the heart, though the pulse rate was 150 per minute. The child did not speak and did not fight the nurse but exhibited automatic movements of suction, mastication and dancing or marching round and round. Collet suggests that the effect of the cocaine was to bring about relative inhibition of the cortex, which accounts for the mutism and the predominance of the action of the optostriate body, which presides over the elementary movements for self-preservation: suction and mastication.

DENNIS, San Diego, Calif.

TWO CASES OF FAMILIAL CEREBROMACULAR DEGENERATION PREVIOUSLY PRESENTED AS CASES OF LEBER'S DISEASE. W. B. INGLIS-POLLOCK, Ann. d'ocul. **171**:449 (May) 1934.

Inglis-Pollock reports cases of familial cerebromacular degeneration in a brother and sister, beginning at 11 and 8 years, respectively. Progressive amblyopia and changes in the fundi (pigmented macular masses and secondary optic atrophy) were present. Both patients died at 20 years of age. During the last few years preceding death paroxysmal spasms occurred, followed by stupor. Treacher Collins considered cases with changes in the macular region as a particular type of retinitis pigmentosa unrelated to Tay-Sachs' disease, which is a familial disease affecting young Jews. In Tay-Sachs' disease there is degeneration of the ganglion cells, and ophthalmoscopically there is no pigmentation of the macular region.

BERENS, New York.

News and Comment

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY, INC.

A meeting of the Board was held in Philadelphia on June 7 and 8, 1935, and examinations were given to thirty-one candidates for certification. Twenty-one certificates were granted; six candidates failed, and four were conditioned. In addition, certificates were granted to thirty-four candidates on the basis of their records without examination. The names of the candidates to whom certificates were awarded are:

Without Examination.—In Psychiatry and Neurology: Harold A. Bancroft, Hartford, Conn.; Thomas M. Barrett, Marion, Ind.; Louis Casamajor, New York; Franklin G. Ebaugh, Denver; Walter Freeman, Washington, D. C.; George A. Gosselin, Hartford, Conn.; George W. Hall, Chicago; Titus H. Harris, Galveston, Texas; J. Allen Jackson, Danville, Pa.; Smith Ely Jelliffe, New York; Baldwin L. Keyes, Philadelphia; Adolf Meyer, Baltimore; Walter Joseph Otis, New Orleans; Mortimer W. Raynor, White Plains, N. Y.; Hans H. Reese, Madison, Wis.; Irving J. Sands, Brooklyn; Arthur J. Schwenkenberg, Dallas, Texas; H. Douglas Singer, Chicago; Carrol C. Turner, Memphis, Tenn.; Otto G. Wiedman, Hartford, Conn.; Edwin G. Zabriskie, New York; Lloyd H. Ziegler, Albany, N. Y.

In Psychiatry: C. Charles Burlingame, New York; C. Macfie Campbell, Boston; Clarence O. Cheney, New York; Delmer D. Durgin, Central Islip, N. Y.; Menas S. Gregory, New York; Arthur H. Harrington, Providence, R. I.; Seth F. H. Howes, Howard, R. I.; James Vance May, Boston; Arthur P. Noyes, Howard, R. I.; Arthur H. Ruggles, Providence, R. I.; Rock Sleyster, Wauwatosa, Wis.; Raymond G. Wearne, Central Islip, N. Y.; William Alanson White, Washington, D. C.

With Examination.—In Psychiatry and Neurology: A. E. Bennett, Omaha; Hugh Thompson Carmichael, Hartford, Conn.; Clarence C. Hare, New York; M. Ralph Kaufman, Cambridge, Mass.; Roland P. Mackay, Chicago; Curtis T. Prout, Hartford, Conn.; Richard B. Richter, Chicago; Jackson M. Thomas, Waverly, Mass.; A. R. Vonderahe, Cincinnati.

In Psychiatry: Robert S. Bookhammer, Philadelphia; Donald M. Carmichael, Brentwood, N. Y.; Joseph H. Conn, Baltimore; Samuel Feigin, New York; Kenneth Keill, Brentwood, N. Y.; H. Beckett Lang, Brentwood, N. Y.; Bradford J. Murphey, Colorado Springs, Colo.; Kenneth J. Tillotson, Waverley, Mass.; Lawrence F. Woolley, Towson, Md.; Carl P. Wagner, Hartford, Conn.

In Neurology: Paul C. Bucy, Chicago; Dean Hume Duncan, Shreveport, La.

Society Transactions

NEW YORK NEUROLOGICAL SOCIETY

Regular Meeting, Dec. 4, 1934

ISRAEL WECHSLER, M.D., *President, in the Chair*

THE RELATION BETWEEN CHRONIC ANTERIOR POLIOMYELITIS OR PROGRESSIVE SPINAL MUSCULAR ATROPHY AND AN ANTECEDENT ATTACK OF ACUTE ANTERIOR POLIOMYELITIS. DR. LEON A. SALMON and DR. HENRY ASLOP RILEY.

The subsequent development of chronic anterior poliomyelitis or progressive spinal muscular atrophy in persons who have had an attack of acute anterior poliomyelitis is a clinical phenomenon which has received little attention in the English medical literature. The foreign literature, however, contains a sufficient number of reports of cases to render the supposition of a causal relationship highly probable. That the nervous system is rendered vulnerable to subsequent disease by an attack of acute anterior poliomyelitis was pointed out by Vulpian and Charcot, but only in the case of progressive muscular atrophy or chronic anterior poliomyelitis does the frequent relationship attract attention.

During the past year 3 patients have come to our attention at the New York Neurological Institute with unquestionable evidence of chronic anterior poliomyelitis or progressive spinal muscular atrophy following many years after an attack of acute infantile paralysis. The evidence of acute anterior poliomyelitis in these patients was present in the lower extremities and was indubitable, the clinical appearance of the affected limb being absolutely typical of that seen in cases of antecedent acute anterior poliomyelitis. In case 1 the onset and course of the second disorder were typical of chronic progressive poliomyelitis; fibrillary contractions were noted throughout the muscular system. In case 2 there had been several apparent recrudescences of a chronic inflammatory or degenerative disease appearing in one region and going on to complete atrophy of the affected group of muscles and then appearing in other regions with the same course. The evidence of the chronic process was not, however, limited to the lower extremities but was widespread. Case 3 represents the type described by several authors in which the second disease appears apparently as a result of excessive demands made on the nerve cells, which perhaps are only mildly injured by the acute poliomyelitis but are deprived of the inherent vitality necessary to maintain them during the span of the patient's lifetime.

In attempts to explain the relation between the two diseases, the expression *locus minoris resistentiae* has been resorted to in many instances. The possibility of a smoldering infection with an ultimate flare-up has had its partisans. Though recognizing how meager are the data on which to found a hypothesis, we believe that the situation may be looked on as premature death or abiotrophy of those neural elements which had suffered sublethally during the attack of acute anterior poliomyelitis. The question is raised whether every case of progressive muscular atrophy may not be referred to an antecedent acute infantile paralysis, regardless of the history presented by the patient. When one considers the frequency of acute anterior poliomyelitis and the elusiveness of its abortive forms, the hypothesis acquires a degree of possibility which warrants further study in this direction.

DISCUSSION

DR. RICHARD BRICKNER: In 1870, Marie saw a patient with multiple sclerosis who three years before had had typhoid. On the basis of this case he formulated

a theory of the origin of multiple sclerosis, namely, that it was the tertiary stage of an infectious disease, such as typhoid, and he compared this supposed tertiary stage with what he knew of syphilis. This idea, so far as I know, has been largely dropped from neurology, and I have wondered since reading Marie's paper whether it would not be a fruitful thought to keep in mind—not in connection with multiple sclerosis but in connection with some other conditions. Epidemic encephalitis, with its supposed relation to influenza, naturally occurs to me. The cases of Drs. Riley and Salmon also suggest Marie's idea.

I wish to ask the authors if they have used poliomyelitis serum in these cases, and if so, what has happened?

Dr. Louis Casamajor: Such cases as these have been reported since the time of Charcot, and it has not been believed that they have anything to do with progressive muscular atrophy. The small number of cases of poliomyelitis with later muscular atrophy and the large number of cases of poliomyelitis in which atrophy does not develop later make the possible relationship between the two hard to credit. However, these cases present sufficient problems to make one stop and think. It is known that encephalitis may be a chronic disease. May not poliomyelitis also be a chronic disease? For years certain muscular atrophies due to disease of the anterior horns have been spoken of as chronic poliomyelitis in spite of the fact that no inflammatory reactions have been described in these cases. One wonders whether this specific atrophy of nerve cells might not be due to a specific toxin; certainly no known toxin is as specific for the horn cells as the toxin of acute anterior poliomyelitis. I was wondering whether any work has been done on the presence of immune bodies in the blood in Drs. Salmon and Riley's cases. It would be important to know whether these patients have acquired as many immune bodies against the virus of poliomyelitis as one finds in ordinary cases of poliomyelitis in which recovery has occurred. There are about three times as many immune bodies in persons who have recovered from poliomyelitis as there are in adults of the general population. Is it possible that these patients have a small number of immune bodies and that they have not acquired sufficient immunity to the disease and are chronic carriers of the poliomyelitis organism? Should the number of immune bodies be much reduced I think that one might look on the condition as chronic anterior poliomyelitis—the end-result of nerve cell poisoning from a disease which has not been overcome.

Dr. Bernard Sachs: I have seen some cases of spinal progressive muscular atrophy that have followed earlier attacks of infantile paralysis. The surprising thing is that this does not happen much oftener. Looked at from an anatomico-pathologic point of view, if the inflammatory process attacks the anterior horn cells in cases of poliomyelitis and of this spinal form of progressive muscular atrophy it would be natural to find that a degenerative process is set up in the course of time.

Dr. Leon A. Salmon: No experiments have been carried out along the lines suggested by Dr. Casamajor.

The question in these cases is whether there is a smoldering infection or a purely degenerative process dependent on decreased vitality of the anterior horn cells as the result of antecedent disease. I hold the latter hypothesis, although there are no substantial grounds for making a choice. Such a view may be succinctly expressed as "acquired abiotrophy."

Dr. Brickner's discussion brings to mind that a Russian author, Zakartchenko, suggested the analogy to the so-called metasyphilitic diseases.

Treatment of the Stutter Type of Personality in a Medical-Social Clinic. Dr. James S. Greene.

The National Hospital for Speech Disorders opened its doors seventeen years ago. Thousands of young men and women have availed themselves of its clinical

services, 70 per cent of whom were given free treatment. More than 15,000 stutterers besides several thousand persons with other speech defects have been treated.

Stuttering may be defined as a phenomenon characterized by tonic and clonic spasms of the vocal tract which result in conversational difficulty and hesitancy. Theoretically it is assumed that the person with the stutter type of personality is one born with a special organic structure and having constitutional factors which all but parallel the constitutional factors of the nonstutter type. The stutterer is an extremely sensitive person in whom the emotional range always overreaches that of the nonstutterer. This human being does not always stutter. An environment of opposition accentuates the conflicts to which he is conditioned and evokes stuttering in its various forms; a neutral or favorable environment does not provoke stuttering. The antagonistic environment may be encountered either in early childhood or in adult life. Consequently, a particular kind of unfavorable environment may evoke stuttering from this person with the organic stutter type of personality either in childhood or in adult life. A specially created favorable surrounding, such as the medical-social clinic at the hospital, is the means by which the stutterer is unconditioned. That is to say, he is brought back to his initial or prestuttering state of security. My paper deals with the description of this special environment and a method of unconditioning the stutterer.

Opinions agree that stuttering is an emotional personality problem (Blanton, Brown, Solomon, Clark and West). Years ago I stated that the problem is centered in the field of human emotions. The adult stutterer usually gives a history of having been a nervous, fearful, unduly irritable and excitable child, often living in a psychoneurotic parental atmosphere surcharged with nervous tension. Such is the fertile soil in which the stutter type of personality is cultured. From early childhood conflicting emotions rule the stutterer's mind. His normal impulses are inhibited. He is a victim of dread, even of terror, so that in the plastic years his doom is practically sealed. His personality development undergoes an ebb and flow which tend toward disintegration. In adult life the fears and feeling of desolation, associated with the speech defect, permeate every field of thought and of activity. No one knows him as he really is. The attributes of his personality make no impression, because his stuttering is the focal point of interest. In short, stuttering is a pernicious handicap which numbs the heart, distorts the processes of the mind and paralyzes normal impulses with a searing sense of inadequacy.

In and around Greater New York alone the challenge is staggering. Of the 6,000,000 inhabitants, approximately 20,000 are adult stutterers. The report of the White House Conference on Child Health and Protection shows that 200,000 children stutter and that only 1 of 10 recovers during the elementary school period.

The therapy applied at the clinic has undergone many modifications and extensions. It is best described as a composite therapy of medical, psychologic, reeducational and social nature, the essential feature of which is the group approach. The aim is to treat the stutterer's whole personality. Group psychology has proved practical because, beyond a certain point, the individual problems of the stutterer become the problems of all. With children, speech training and methods of correction are carried out under medical supervision in school-clinic classes, in the form of a socializing task. In order to give equal opportunity to all, adults must be dealt with en masse. In the medical-social clinic experience has taught that the initial interview is of far-reaching importance. The stutterer is next given a physical examination and then a speech test. For that purpose there is a fully equipped radio department. Then he is examined by a psychologist. Special tests given the patient afford an idea of the mental capacity.

How to reintegrate the disorganized personality is the problem. This must take place so that the essential personality traits are placed in their proper relationship. Throughout the treatment the interest of the physician and of the patient must be focused on the total personality.

Although there may not be any inherent virtue in speech work, it is the only medium for correcting vocal maladjustments. Technical faults respond to reeduca-

tional pressures, not to theoretical discourse alone. The physiology of breathing is easily explained and comprehended so that a normal calm manner of breathing is readily adopted. Breath control is a great factor in emotional control. Muscular relaxation and coordination are important group activities which the stutterer finds hard to master. Depending on the degree of the excessive and inconsistent emotional discharge, the stutterer shows pronounced differences when compared with the nonstutterer in the responses of muscular contraction and relaxation. The majority of stutterers bring into play unnecessary and excessive movements and find difficulty in controlling fine and gross movements. Mothers complain that the stuttering child talks and walks badly and is fearful and clumsy in all things. Adults complain of jerky muscular movements, which demand excess energy. Their actions are spasmodic and unnecessarily repeated. Thus there are stuttering musicians, who repeat the same notes several times, stuttering typists, etc.

Group activities of rhythmic coordination exercises are done to music. Groups of stutterers are taught to combine and alternate muscular contractions with progressive degrees of relaxation. They acquire a certain amount of abandon which, in turn, is reflected in speech.

Every stutterer's life is one of introversion, repression and frustrated desires. Infantile attitudes and conflicts remain with him. He finds no satisfactory solution for his problem. The psychiatrist's task is to discover the underlying chain of causes. He must replace the infantile attitude with an adult one. A departure from the traditional therapy is necessary. The problem is rather intricate and not easy.

Psychoanalytic treatment of the usual type, wherein one tries to express thoughts in words, is an almost impossible task for a stutterer. The acquisition of freedom and rapport between the analyst and the stutterer is a slow process. Patients who have been subjected to psychoanalysis before coming to the clinic claim that the procedure is long and costly and has not been productive of the desired results. While the analyst sits silently by the patient struggles with free associations and finds transference difficult. Moreover, the analyst seldom reaches the constructive phase of treatment. This form of therapy is psychic only and is not complete without the physical reeducational program. I know many stutterers who during analysis kept asking themselves, "When will the doctor do something for my speech?" In every stutterer's case the defective verbal production is a fixed and living thing and, as pointed out, every form of treatment must consider that phase in actual practice.

The specially created atmosphere of the clinic is one in which informality, encouragement and sympathy hold sway; it radiates calm, peace and tranquillity. The stutterer is put at ease in such a way that perhaps for the first time he appreciates a hitherto unknown spiritual peace. In such surroundings the psychoneurotic symptoms, which complement the stuttering speech, respond readily to direct and indirect suggestion. The old habits of a nonsocial, egocentric, fearful personality are broken down. Feelings of shame and secretiveness are brought out into the open. To effect this, a special procedure has been introduced. I call it "open door" or group psychiatry, and it has proved to be practical and beneficial. The patient consults with the physician in a large room, the door remaining open. It is possible to insure a sense of privacy by placing the desk at the far corner of the room. In spite of the open door it is amazing how quickly the patient adjusts to this "open door" psychiatry and is not perturbed. Minor emotional disturbances and even major conflicts are successfully resolved. However, when deemed necessary, a closed door interview is given, so that unconscious difficulties that have been evaded are brought under control.

The open door method has one valuable asset. It makes it possible to call in other patients who happen to pass the open door and to utilize them in various ways. Their presence is most helpful; when necessary, they serve as eager listeners or they participate in the discussion. The personal aspect of secret problems is eliminated, and the patient realizes that these problems are not his alone but belong to the stuttering fraternity as a whole. Almost unbelievable

reconstruction takes place within a short time, and an integrated personality then comes into being.

Since stutterers are afraid "to go places and do things," in brief, afraid of social contacts, the situation is reversed by bringing society to the stutterer. In the clinic all patients automatically become members of the clubs. There are debating and literary clubs, a dramatic club, a class in journalism and a choral singing club. The activities arising from these are periodic dinners, entertainments, dances, outings, etc. Wednesday evening is devoted to an important meeting of the entire clinic. It takes the form of a business meeting. The speeches are short and voluntary. Occasional criticism and constant encouragement are the order. A great deal of practical psychology is put into these meetings; each patient is in the presence of his fellow stutterers, among whom is always some one worse than he is; he goes through a speech crisis—a kind of spiritual uplift—and thereby secures his first hold of confidence in a speech situation of a vital nature. Here he emerges from his introverted shell in a form of spiritual conversion; faith and belief in himself become crystallized and establish the foundation which recondition him to subsequent social contacts.

The dramatic club gives the patients additional opportunities for social adjustment. A group of former stutterers are now giving little plays in the different settlement houses around town.

To summarize: 1. The person with the stutter type of personality is born with a highly emotionalized organic structure. 2. Only an antagonistic environment to which he becomes conditioned may evoke stuttering. 3. The problem is primarily one of psychologic reconstruction, emotional control and integration. 4. The vast number of stutterers requires special group treatment in a specially created environment wherein they acquire spiritual calm. 5. The most practical agency for unconditioning the stutterer is one comprising medical, psychologic, psychiatric, reeducational and social therapies, which have been developed in the medical-social clinic.

PSYCHIATRIC ASPECTS OF SPEECH DISORDERS. DR. SMILEY BLANTON.

Speech is a delicate indicator of the normality of the brain and the nervous system and of mental development. The function of speech is to express emotions and to adjust oneself to other people. The infant passes through four stages of speech development. He makes many more sounds than are necessary for English speech. In all the speeches of the world there are about 600 sounds; in English speech there are about 60 sounds. Delayed speech is caused by lack of development of the brain (primary amentia), by injuries to the brain (secondary amentia) by deafness and by prolonged duration of infantile speech. Speech training in these cases must be given in the form of games and not through rigid drills. Stuttering is a fear neurosis. The symptoms are caused by a release of inhibitions having to do with the primitive movements of suckling, swallowing, vomiting, etc. which involve the oral muscles. Stuttering is only a symptom, and to treat it properly one must reeducate the stutterer.

DISCUSSION ON PAPERS BY DRS. GREENE AND BLANTON

DR. LOUIS CASAMAJOR: I have reached the conclusion that Drs. Greene and Blanton are both right, and I am certain that if Dr. Orton were here to give his point of view I should feel that he is right too. The question is, are they all talking about the same thing? I doubt very much that they are. When one considers the question of stuttering one is grouping into one category a number of conditions which are probably essentially very different. In the old days one used to try to distinguish between the stutterer and the stammerer. I never could discover what was meant by that, but there was an idea behind it—an attempt to divide speech defects into two groups.

There is no doubt that Dr. Greene secures interesting results in his work. I have no doubt that Dr. Blanton obtains just as good results; I believe that good

results may be obtained in certain cases by the phonetic drills that both Dr. Greene and Dr. Blanton seem to disparage. Again the special type of training which Dr. Orton employs brings results. They do not all secure results in the same cases. It is probable that in the cases in which Dr. Greene obtains such splendid results Drs. Blanton and Orton might fail and that Dr. Greene might secure no results in the cases in which Dr. Blanton obtains cures.

Dr. Greene spoke of the "stuttering personality." There is no doubt that there are stutterers of the kind which he described, and they are the ones with whom he obtains the best results. This type of stutterer is inept in his motor system and in his social contacts; he draws away from society simply for the reason of his ineptitude rather than for the stuttering alone. This type of person is seen strikingly among persons with congenital double choreo-athetosis, in whom motor ineptitude is very great. Often this type of stutterer has what Dr. Blanton spoke of as delayed speech, not talking until he is 5 or 6 years of age. By muscle training alone such patients begin to speak better and obtain increased synergic control of their vocal musculature; all they need is training of that sort which will make them more adept in what they do. Dr. Greene's patients, in addition to having a motor ineptitude, have a social one. They do not want to meet society because they are inadequate to face it as it exists, not only on account of their speech defect but on account of what Dr. Greene means when he says the "stuttering personality." What I understood from him was that stuttering is only a symptom of a general personal maladaptation to life. All stutterers do not come under that class. There are many stutterers who have no social ineptitude and no muscular inability. I am thinking of bad stutterers who have had all kinds of treatment—intelligent persons, e. g., expert pianists with a musical ability which speaks for a high degree of coordination.

Dr. Blanton's cases of delayed speech are of extreme interest, and he has included these to bring something else into the picture besides the stuttering itself. He describes different kinds of stutterers from those Dr. Greene has spoken about. These are the stutterers in whose cases the cause lies more deeply from a psychiatric standpoint. I agree with Dr. Blanton that these patients are psychoneurotic. There is a fear core; in many of the cases the condition passes from the simple fear neurosis into the compulsion neurosis. There are other stutterers too who are definitely schizophrenic. They are definitely more shut in and less social. In a consideration of stuttering, therefore, there is a manifold group of persons with a single common symptom of ineptitude in speech. They extend from the simple stutterer of whom Dr. Blanton has spoken (the child who was cured by opening the window) to the personalities Dr. Greene described, up through the person with psychoneurosis to those with compulsion neuroses and with the more severe schizophrenia.

Dr. E. D. Friedman: I wish to express my appreciation of the striking results which Dr. Greene presented this evening and of his point of view. He has brought out the salient feature of stuttering, namely, that the patient suffers from an inferiority complex, perhaps due to the dominance of a tyrannical father or to a conflict in other emotional situations. What Dr. Greene has really done is to take this person out of an atmosphere in which he feels inferior and bring him in contact with a group that will give him an opportunity for the expression of the herd instinct on a level of equality with others.

As an organicist, I wish to draw an analogy between stuttering and what is known as striatal speech. Striatal speech is very similar to the speech of the stutterer; following Wilson in his study of the physiology of the basal ganglia one sees, as a result of the feeling of inferiority or of a fear neurosis, such a person making a recession to the level of the basal ganglia. That this is possible seems to be indicated by the associated release movements (chewing, smacking and excessive respiratory efforts) which accompany such speech; in other words, they are release phenomena which have been brought to the surface owing to the dominance of the basal ganglia and the lack of cortical control. Similar speech disturbances are observed in cases of severe chorea, athetosis and Wilson's disease.

I am much interested in Dr. Blanton's reference to the teaching of speech in conjunction with an act or an object. That brings the whole question of speech into relationship with the work which Goldstein of Frankfort has done. He views speech as a *Gestalt* phenomenon, namely, that speech is the expression of a situation or constellation of things; in this way the child learns the rudiments of speech, and the adult likewise makes use of speech to express a *Gestalt*.

The fact that the inferiority complex does play a rôle in some cases seems to be borne out by the case which Dr. Blanton mentioned. When the man put on his dress-suit his stuttering stopped; he increased his ego and overcame the inferiority situation. I presume the same thing would be true of the man who makes a good speech after he has had a little alcohol; as a result of stimulation from the alcohol he sheds the feeling of inferiority.

In conclusion, one may say that both speakers, each in his own way, brought forth evidence to prove their theses and that they have thrown a great deal of light on some of the mechanisms which underlie the phenomenon of stuttering.

Dr. Bernard Sachs: The discussion has left one happy impression: that stuttering is curable. I think that those who have been in practice for many years will agree that stutterers are difficult to deal with and from many points of view seem almost hopeless. I find little disagreement between the two speakers this evening. Dr. Blanton had a much larger subject in mind than Dr. Greene, including within his subject speech disorders dating back to early infantile cerebral palsies. I daresay the methods which Dr. Greene employed in his cases would hardly be applicable in cases of early speech disorders due to lesions of the brain. There is no doubt that as far as stuttering is concerned both essayists agree fundamentally that the difficulty about stuttering is a fear neurosis, and I think that when that is said as much has been said as is worth saying and as much as is definitely proved with regard to the psychologic aspects of stuttering.

I have been a witness to the work which Dr. Greene is doing, having spent some time with him on one of his memorable Wednesday evenings; nothing within the last ten years has made such a deep impression on me as the success which Dr. Greene has achieved in these cases of stuttering. Some psychiatrists would differ in their opinion as regards the psychiatric factors in stuttering, but from the practical point of view the fact that stuttering can be cured seems to me a splendid achievement. Of course some stutterers are more resistant to cure than others. In Dr. Greene's clinic he has actually organized a club for stutterers, and the fact that they all feel they are in the same plight, that one man cannot reproach another because he does not speak distinctly and that they are all in sympathy with one another has a great deal to do with their success. In the demonstration given here they all applauded each other. They felt satisfied that there was one of them who showed what they were able to do. This medical-social clinic is a success. I remember the man who had been a stutterer for thirty-seven years. He had more difficulty when I first heard him than he had today. It is remarkable to see what the practical effect of this procedure is. Many of these persons were utterly unable to occupy responsible positions, no matter how competent they may have been; in the case of some of the young women it is remarkable to see how capable they are, when they never would have been able to advance even in secretarial work; they are now perfectly able to take their places with their equals in every form of social and business activity. It is a medical-social clinic. I like the wording. The medical-social club which Dr. Greene has formed seems to me to be an important element in this. Of course, the other factors which he has introduced, the coordinated exercises, etc., are all helpful. In my opinion it is most important to encourage this work in every possible way, and I am happy to say that I now believe that stuttering is a curable condition; there is no excuse for any one stuttering if he can find proper treatment. The treatment should be begun as early as possible.

Dr. Paul Schilder: One must congratulate the men who have made such a determined effort to develop a proper technic in treating persons with psycho-

neuroses of speech. Similar efforts are needed for the treatment with other types of neuroses. One does not know what to do with a person with a neurosis who for one reason or another cannot be submitted to psychoanalysis, nor has any determined effort been made to come to a real understanding of the methods to be used in the shorter treatment of these patients. One of the problems which stands out in the discussion as of fundamental importance in the treatment of every neurosis is: Should one treat the "periphery," the organ as such, or the total personality? The avenues of approach seem to be opposite to each other, but this is only apparently so. There are no isolated organs. The training of an organ can be carried out only by training the whole personality. In every organ something of the total personality is reflected, and treatment of the organ will affect the total personality. There is another important point in this connection; it makes no difference whether one treats symptoms referable to a viscus which is organically sound or not. The organ is always a part of a personality, even though it is the site of organic disease. The treatment of persons with certain types of disorders due to encephalitis or to a cortical process is not different from that given to any neurotic patient.

Among the methods which have been emphasized as fundamental are the use of play, the emphasis on worth-while aims and finally the treatment of the personality. All these methods approach human beings in a special setting of society. They are social methods, based on the identification of one person with others, and are related to the aims of the person in society. In this respect I see enormous progress in the treatment of persons with neurotic speech disorders compared with the progress made in the treatment of persons with neuroses by other methods. Persons with neuroses are not treated in groups, as they should be. The individual problems of the neurotic person are placed in the foreground too much. He is not seen in his social environment. When one sees a patient, one is careful to keep other patients from knowing about their common problems. I think that is wrong. I have tried repeatedly to discuss the problems of one patient in front of other patients. Why not? All are human beings. The problems are essentially the same, and if one can show the patient that his problem is common to all and expresses itself in one way with him and in another way with the next patient, one cannot say what the results of such free discussions of fundamental human problems in groups may be. I can only say that the patients enjoy these discussions so far. I think I do get results, but the method needs elaboration. I congratulate the men who have worked with speech disturbances and are so far in advance in developing a proper technic.

Dr. Philip R. Lehrman: Without minimizing the dramatic therapeutic demonstration given, I wish to emphasize that methods which aim at therapeutic results only have not solved problems of etiology and prevention. Often the achievement is merely the removal of a symptom, and mankind has used such methods for a long time when dealing with neuroses en masse. Each neurotic symptom, though apparently isolated, is related to a basic difficulty in the patient, and what is common to all is the symptom of being "asocial." Thus a special social structure was reared by religion, and its rituals and rites did much for the compulsions and obsessions. Aggression, always a source of danger in a human being and a potential nucleus for symptom formation, is exploited by mass enthusiasms, as can be seen in recent history. Only psychoanalysis was able to throw light on these means of mass therapeusis, and it has also given the meaning and origin of the symptom itself. In his "Psychopathology of Everyday Life," Freud explained lapses in speech and thus gave impetus to the deeper study of some neurotic speech disorders. Dr. Blanton, who has followed this subject further, has indicated that the inhibition of the speech function is similar to the inhibition of other functions which are neurotically involved, such as locomotion or potency. In applying the methods of psychoanalysis in a few selected cases he promises to reveal the genesis of neurotic speech disorders.

Dr. James S. Greene: Every one seems to agree that stuttering has an emotional origin and that it is a personality disorder. The stutterer's fear is exaggerated; pathologic fear rules him. Of course one would like to know the "why" of all this, and there is difference of opinion concerning it. I suppose some day the basis will be found and there will be general agreement.

Regarding treatment, I think that, no matter what form it takes, if it produces results it is good treatment. Psychoanalysis is good but cannot be carried out. Group psychology is the answer on account of the large number of persons requiring treatment. In Greater New York alone there are about 50,000 stuttering school children and, I think, about 20,000 stuttering adults. Recent statistics show that there are about 1,000,000 stutterers in the United States. How about those who cannot afford to go to a psychoanalyst? Hundreds of young men and women come to the clinic who cannot hold a $5 job.

When I opened the clinic seventeen years ago, I was interested in causal factors, but the further I went into the problem the more I realized that what the patients needed most is immediate relief from social conflict, their fear neurosis, and, as Dr. Friedman pointed out, a rejuvenation of the herd instinct had to take place. Amalgamated group therapy takes care of all this.

Dr. Casamajor brought out the fact that stutterers have a social ineptitude and also he contended that stuttering involves many different kinds of mechanisms and has many different kinds of meanings. I believe that the stuttering syndrome always has the same basic meaning, a fear or anxiety reaction. Its extent and secondary manifestations are naturally modified by other factors, psychologic and constitutional. While the stutter type of personality may take on many forms, and the total clinical picture vary considerably in each individual case, still the anxiety or fear neurosis always stands out as a definite entity.

Dr. Smiley Blanton: Those who discussed the papers have made helpful suggestions. Dr. Friedman's suggestion that the physiologic cause of a stutter was the breaking through of the primitive patterns of the basal ganglia accords with my theory of the cause of stuttering, which was published in an article in 1926. I am more convinced than ever that this theory is true. I formulated it after my experience during the World War in neuropsychiatric work. Most of the men who had real "shell shock," that is, who were blown up by a shell or knocked down by a bullet, etc., could not talk for a time; sometimes their reflexes were gone; their sphincters were no longer under control. Apparently the cortex no longer controlled the basal ganglia; these "shell-shocked" soldiers acted the same way as a child does who has an injury of the cortex.

There are several types of stutterers: the type that has a compulsive fear neurosis, the manic-depressive type and the schizophrenic type; there are a few persons who stutter as a result of organic injury of the brain, and there is the "tic" type. In some of these cases it is clear the emotional difficulty does not invade the whole personality. The stuttering symptom seems to block off the emotional difficulty so that it has only a localized effect. I know several middle-aged persons who stutter badly, but who are getting along well and are well adjusted and happy. Apparently the stuttering has not affected their personality.

I realize, as everyone does, that psychoanalysis is not a suitable method for treating the average neurotic person. In the first place there are not enough psychoanalysts to do it; also it is too expensive, but what the psychoanalysts may try to do is to bring out new facts which can be used in the treatment of the stutterer from the psychiatric point of view. If it does that it accomplishes what one hopes to do. Unless treatment can be reduced to a more scientific basis, it seems to me that cures may be secured but not prevention. For example, inferiority complex is a term which is helpful, but would it not be better if one could reduce this to a lower common denominator and see what is meant by a feeling of inferiority? That is what psychoanalysis tries to do. It may prove inadequate, but it seems to me that it does bring out facts which are useful in treating the stutterer. But above all, psychoanalysis gives some facts which will help to prevent this difficulty or to cure it in the earliest years.

PHILADELPHIA NEUROLOGICAL SOCIETY

Dec. 21, 1934

D. J. McCarthy, M.D., *in the Chair*

A Case of Tuberous Sclerosis With Unusual Clinical Findings. Dr. Ralph L. Drake.

A boy of Polish descent, aged 12 years, was admitted to the neurologic dispensary of the Germantown Hospital with the complaint of convulsive attacks, dizziness and headache. Birth was normal and at full term. The child walked at the age of 13 months and talked at 20 months. He was apparently well until the age of 4, when there was a nocturnal attack of unconsciousness without convulsive movements. There was marked respiratory embarrassment accompanied by general cyanosis, biting of the tongue and frothing at the mouth. This lasted five minutes and was followed by a period of somnolence. The child was well until one year later, when he had an attack while in bed consisting of a sensation of feverishness, headache and visual hallucinations. The last consisted of a hallucination of caterpillars crawling along the wall. He was not unconscious and immediately went to sleep; on awakening he had complete memory for all that had happened. About one year later he had a similar attack accompanied by visual hallucination of Negro boys fighting. After this he had several epileptiform convulsions at intervals of five or six months. During the period from 1926, when he was 4, up to the present he has complained frequently of headache and dizziness. Occasionally there has been diplopia. There have been no motor weakness and no other sensory disturbances. On Nov. 19, 1934, he had another attack in which the face was flushed and there was a rise in temperature to 105 F. He complained of stiffness of the right arm and leg, rigidity of the neck and generalized muscular twitchings. Twenty-four hours later he noticed that the light in his room appeared brilliant green, and changed about one hour later to deep blue. This attack lasted for three days. Examination on the last day revealed no neurologic changes except nystagmoid movements bilaterally.

The mother said that the patient began to attend school at the age of 7 years but has reached only the third grade. Within the past year or two he has shown a marked degree of mental irritability, has become seclusive and prefers to play with younger children. Within the last month schooling has been discontinued because of inattention and restlessness.

There is a definite degree of mental retardation. Degeneracy is manifested by presence of a high, narrow palate and changes in the optic disk. The latter consist of elevation of the upper half of each disk about 2 diopters above the lower half. This is due to an anomalous formation of the disk. There is no adenoma sebaceum and no evidence of a retinal tumor. The visual fields are normal.

Encephalographic studies by Dr. Fay in 1932 showed three small discrete masses of calcification in the left occipital area and a similar single spot of calcification on the right side. The third and fourth ventricles and the aqueduct were apparently normal. There was a bulging of the right thalamus into the right lateral ventricle. The basal cisterns were increased in size, and the air pattern over the convex surfaces suggested the presence of microgyria.

The Bárány test (performed by Dr. Winston) showed disproportion between the duration of nystagmus and the duration of vertigo after turning and an appreciable loss of function of the entire vestibular mechanism on both sides after caloric stimulation. These findings were suggestive of supratentorial abnormality.

The presence of a definite degree of mental retardation, convulsive phenomena, developmental anomalies and multiple cerebral lesions in a child speaks for the presence of tuberous sclerosis. Calcification in the case of a true glioma or tuberculoma does not accord with the clinical picture. The visual hallucinations and rise in temperature are not easily explained. The most probable location of a

lesion producing the rise in temperature would be in the hypothalamic region; or this might be explained on the basis of a subependymal nodule acting as a ball valve and producing sudden dilatation of the third ventricle with resultant pressure on the hypothalamus. The visual hallucinations are difficult to explain. The unformed visual hallucinations might be explained on the basis of lesions of the occipital lobe, but this hardly accounts for the true formed hallucinations of figures which, according to Horrax and Putnam, occur only in cases of lesions of the temporal lobe affecting the optic tracts in that location or by an invasion of the pulvinar of the thalamus. The encephalographic evidence of bulging in the region of the right thalamus is in favor of such a thalamic lesion in this case.

DISCUSSION

Dr. R. Matthews: Tuberous sclerosis is generally considered to be rare in this country, but among 335 feebleminded children 304 were thought to have tuberous sclerosis. Some have other lesions such as those producing marked mental deficiency without convulsive seizures, and one child had what appeared to be adenoma sebaceum.

Dr. N. Gotten: I made the encephalogram in the case presented. The case was reviewed in conference, and the consensus was that the condition was tuberous sclerosis.

Multiple Cerebral Emboli. Dr. Frederic H. Leavitt.

I present the uncut brain of a patient who died in the psychopathic service of the Philadelphia General Hospital about six weeks ago. The pathologic features are: (1) a large scar in the cortex on the left side due to thrombosis of an artery in the sylvan fissure (fig. 1) and (2) a large scar in the cortex on the right side due to a thrombus of the posterior portion of an artery in the sylvian fissure (fig. 2). The pia-arachnoid is thickened, especially over the areas of the cortical scars. The left hemisphere shows a marked depression from softening caused by the thrombus of the entire vessel of the left sylvian fissure. The scar extends from the posterior part of the third frontal convolution and involves the parieto-occipital area and the lower half of the entire parietal lobe. On the right side there is a scar resulting from the occlusion of the terminal branch of the artery of the sylvian fissure which has destroyed the greater part of the right parietal lobe. Examination of the base of the brain shows the arteries there to be normal in size and slightly fibrotic but collapsed. The spinal cord appears to be normal except for the evidence of bilateral descending degeneration of the motor pathways.

The patient had been more or less constantly under my care since 1926, and I had the opportunity to examine her closely during these years. She died from exhaustion in a condition of marked dementia. There were pronounced atrophy of all the muscles of the four extremities and "contracture in flexion" of both arms and both legs. The patient was 43 years of age, and for many months prior to death she had been practically completely demented and paralyzed and subject to periods of violent screaming, which were so annoying that it became necessary to remove her from her home.

At the autopsy, in addition to the changes in the brain, there were signs of endocarditis of the mitral valve, the valve being thickened and perforated. There was evidence of embolic areas of softening in the kidneys and spleen.

The patient was studied at the Orthopaedic Hospital in 1926, and on two subsequent occasions at the Graduate Hospital in Philadelphia. Various diagnoses were made, including neurosyphilis, hysteria, cerebral vascular disease from thrombosis and embolism.

The history of invalidism dates from the age of 17, when there occurred an infection of the face which was diagnosed as erysipelas. The endocarditis of the mitral valve without decompensation followed this infection. Shortly after the patient recovered from the infection the cardiac murmur disappeared and was not again observed, despite the evidence of "chronic endocarditis" found at autopsy.

In 1926 hemiplegia suddenly developed on the right side and was accompanied by complete motor and sensory aphasia, with apraxia. Complete recovery occurred within a few months; the patient was able even to return to duty as a stenographer in a busy office. Twenty months later sudden hemiplegia occurred on the left side, without motor or sensory aphasia (the patient was right-handed), and in a few months complete recovery was made from the second "stroke." Altogether the patient had five apoplectic attacks; after the second attack, recovery, both mental and physical, became less and less complete. During the last two years

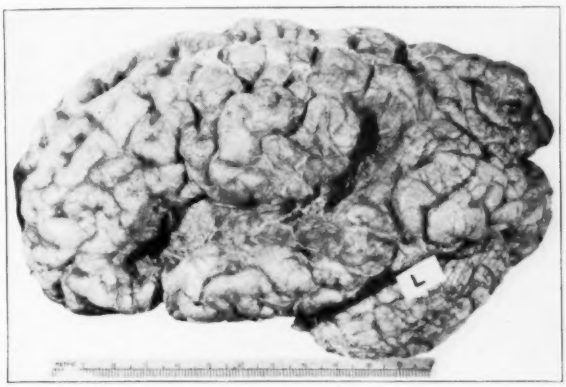


Fig. 1.—Left half of the brain. There is a large scar in the cortex due to thrombosis of an artery in the sylvian fissure.

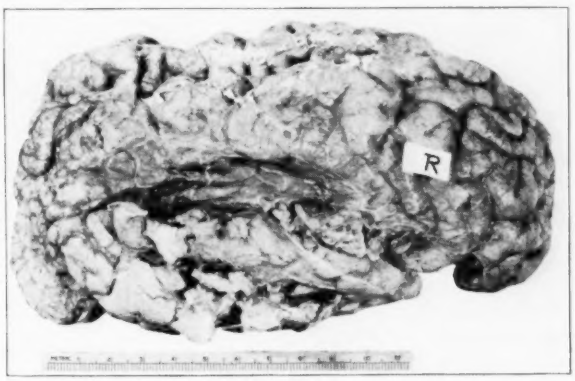


Fig. 2.—Right half of the same brain. There is a large scar in the cortex due to a thrombus of the posterior portion of an artery in the sylvian fissure.

of life the patient became demented, with almost complete motor aphasia, and the atrophy of the extremities began to develop with "contracture in flexion." It was deemed that she was anesthetic to pain and temperature for the reason that she paid no attention to the effects of what should have caused discomfort from pain and heat. On several occasions she was badly burned by hot water bottles and evidenced no signs of discomfort. When stuck with a pin, either accidentally or for the purposes of examination, she gave no sign that such a procedure was uncomfortable. I looked on this not as a mental reaction but as one in which she did not recognize sensations of pain and temperature. The patient was

not deaf after the first two apoplectic attacks, and I do not consider that she was deaf at any time, but she paid little attention to auditory stimuli in the later years of life because of mental deterioration. The diagnosis made at the Orthopaedic Hospital and at the Graduate Hospital was "cerebral embolism," and the diagnosis at autopsy was "multiple cerebral emboli from chronic mitral endocarditis."

The interesting features of the case are the extreme degree of bilateral atrophy of the parietal lobe resulting from vascular occlusion of the arteries of the sylvian fissure by emboli resulting from chronic endocarditis, producing bilateral hemiplegia, marked muscular atrophy, motor and sensory aphasia, marked dementia and, presumably, sensory dissociation phenomena.

DISCUSSION

DR. J. W. MCCONNELL: Did you make an analysis of hearing?

DR. F. H. LEAVITT: I probably did not pay enough attention to the patient's hearing to make a note of it. The patient was examined several times. The spinal fluid on no occasion showed anything indicative of cerebrospinal syphilis or of any other inflammatory condition of the cerebrospinal system. The systolic blood pressure on numerous occasions was not above 140; generally it was about 110. Ophthalmoscopic examination showed no signs of sclerosis and no signs of increased intracranial pressure.

DEVELOPMENTAL DEFORMITY WITH NUCLEAR PARALYSIS OF SOME CRANIAL NERVES. DR. DONALD W. HASTINGS.

A youth, white, aged 19, of German and English ancestry, was brought to the Philadelphia General Hospital by the police on Nov. 23, 1934, and was admitted to the service of Dr. Charles W. Burr in the psychopathic department. The charge against him was that while nude he had gone out in the street at 2:30 a. m. and had chased a woman who happened to be passing. The patient admits he was in the street while nude, but denies the remainder of the charge. He says that once in May 1934 he went into the street naked, but he states that he had been drinking at that time. He cannot explain his actions on this occasion.

The patient's father disappeared twelve years ago; his mother died several years ago after an operation on the gallbladder. He is the only boy of five children and the fourth in line of birth. No other children are deformed. The history as obtained from an aunt and the eldest sister is as follows: The child was born spontaneously and without instruments (the aunt witnessed the birth). The aunt immediately observed that the right hand and foot were malformed and that the right corner of the mouth was pulled downward. Within the next few days it was seen that when the baby slept the eyelids were not closed, but that the eyeballs turned upward; the mouth was never closed, and he seemed to have difficulty in suckling and a tendency to drool excessively. When old enough to observe moving objects he moved his head en bloc to watch them, and when he began to learn to read he moved the entire head to follow the printed line. His face has always been expressionless, and he has never been able to close the mouth completely. He finished the eighth grade at the age of 16. He has never been able to secure a job because of the crippled right hand. He has no symptoms of psychic epilepsy other than the one which brought him to the hospital.

The past medical history includes: influenza at the age of 1 year, successful vaccination at 9 years, measles at 11 years and questionable rheumatic fever at 14 years. There is no reliable history as to whether the mother had any illness during gestation, whether either parent had a chronic disease or whether chemical contraceptives were used prior to this pregnancy.

During the past month in the wards the patient has been well behaved and cooperative. The physical findings are: absence of the middle three digits on the right hand, with the exception of their extreme tips and finger-nails; a blunted great toe and a small toe-nail on the right foot; atrophy on the right side of the tongue, with deviation to the right, and an expressionless face, with open mouth

and a fixed gaze. Further, the patient cannot wrinkle his forehead, close the eyelids, whistle, blow out his cheeks or close the mouth. The eyeballs roll upward, exposing the sclera, when he tries to shut the eyes. Dr. J. C. Siggins reported: "There is paralysis of the orbicularis palpebrarum. The patient cannot completely close the lids. He is unable to diverge, indicating paralysis of the sixth nerve supplying the external rectus muscle. There is also paralysis of the superior oblique muscle. There is partial paralysis of the third nerve. Convergence and rotation of the eyeballs downward and slightly upward successfully indicate some function of the third nerve. The levator palpebrae superioris muscle is only slightly affected. The fundi are normal."

The pupils reacted to light but not in accommodation. The abdominal reflexes were reduced on the right side. The facial muscles showed the reaction of degeneration. All other cranial nerves were intact.

Laboratory studies showed a negative Wassermann reaction of the blood and spinal fluid and a negative colloidal gold curve. The blood count, results of urinalysis, basal metabolic rate, results of the dextrose tolerance test, roentgenograms of the skull, electrocardiogram and blood chemistry were all within normal ranges. A psychometric examination revealed an intelligence quotient of 77, and set the mental age at 12 years and 4 months.

The probable diagnosis is (*a*) some defect in the germ plasm, either sperm or ovum, that produced a congenital malformation of the involved cranial nuclei as well as the deformity in the right hand and foot; (*b*) some infectious disease experienced in intra-uterine life, such as poliomyelitis or an encephalitis, which involved only the medulla, or (*c*) a combination of *a* and *b*.

DISCUSSION

Dr. W. G. Spiller: Recently a Negro child, aged 6 years, came to the neurologic department of the University Hospital, with unilateral facial paralysis. The mother asserted that it had been present since birth and that forceps had not been used. Dr. Ornsteen found the reactions to electrical stimulation so reduced in degree of excitability that it seemed to him probable that the muscles which should have been supplied by the affected facial nerve had never had much reaction to the electric current.

The condition seemed to me to belong to the group described by Möbius as infantile *Kernschwund*. Dr. H. M. Thomas published an important study in which 2 cases of congenital defect of the facial nerves in 2 brothers, aged 21 and 19, respectively, were described. In discussing this paper, I mentioned the resemblance of the cases of Dr. Thomas to the Landouzy-Dejerine or to the facial type of progressive muscular dystrophy.

Dr. F. H. Leavitt: A woman brought a charge against the boy presented here that he pursued her down the street when he was entirely unclothed. He denies the charge and states that he has no recollection of having run down the street unclothed. This same thing had happened about fourteen months prior to this, and he was arrested. Again he had no recollection of the alleged act. My impression is that in view of the findings of organic deficiency he is organically epileptic and that these attacks are epileptic equivalents. He was sent to the Philadelphia General Hospital for observation, and such is the opinion there.

Diabetic Coma: A Clinical and Pathologic Study; Preliminary Report. Dr. Helen E. Riggs and Dr. W. Walter Dyer.

Cases of diabetic coma in which laboratory tests show successful response to treatment yet death occurs are all too frequent. It was with the hope of revealing some factor or factors, in addition to the deranged metabolism, capable of causing death in cases of diabetic coma that this study was undertaken. Six cases from the metabolic division of the Philadelphia General Hospital, service of Dr. E. S. Dillon, form the basis of this preliminary report.

Fatal cases of diabetic coma in which adequate treatment has been given may be divided into three groups: (1) cases of coma plus a complication in itself capable of producing death (e. g., occlusion of the coronary artery); (2) cases of coma plus a complication, serious but in itself not necessarily fatal (e. g., gangrene of the leg), and (3) cases of uncomplicated coma. It was thought that the third group would afford the closest outline both clinically and pathologically of the primary picture.

In the group of cases of uncomplicated coma, 5 of the patients were white and 1 was colored. The ages ranged from 14 to 45, and the known duration of the diabetes, from 3 years to a few months. In no case was there clinical or pathologic evidence of infection of the blood stream. The blood sugar on admission ranged from 278 to 1,500 mg. per hundred cubic centimeters and the carbon dioxide-combining power of the plasma, from 24 to 11 volumes per cent. All the patients received vigorous treatment. The time of death after the beginning of treatment varied from eight to ninety-six hours. Terminal hyperpyrexia and vascular collapse occurred in each case.

Each of the patients presented in addition to the diabetic coma a picture of shock on admission. This has long been recognized and explained partly by Atchley, Peters and others. In 1933 Lande said "two factors, shock and hyperpyrexia, are of importance in the mechanism of fatal diabetic coma." Shock is attributed to loss of blood volume, as evidenced by normal or increased amounts of serum protein, the concentration of hemoglobin and, more recently, direct measurement of the volume of blood by Chang and Hanop. There has been no adequate explanation for the terminal hyperpyrexia, although Lande stated: "It has been of fatal significance for not one of our patients presenting this clinical feature has recovered, and in its presence insulin is without effect." Lande further suggested that the hyperpyrexia may be of cerebral origin.

Postmortem examination did not show any definite body changes, gross or microscopic, to account for the fatal termination. The general pathologists' report was "diabetic coma." The cases were recorded as "metabolic deaths." In the 6 cases in this group there were intracranial lesions which were constant, definite and sufficient to cause death. All the patients showed a diffuse, acute degeneration of the ganglion cell elements, with progressive and regressive glial reaction, mainly of macroglia. There was also proliferation of the mesodermal elements of the meninges. These were secondary to changes in the capillaries and small venules. The capillary bed showed degenerative changes in the endothelium and even lysis of the wall. The small venules showed degeneration in the endothelium and the adventitia, with resulting transudation of fluid.

In the cases studied there were two general types of change in the ganglion cells: (1) swelling and hyalinization of the cytoplasm with loss of Nissl bodies, equivalent to the edematous cell changes of Jakob, and (2) the ischemic cell disease of Spielmeyer, the ganglion cells being shrunken, elongated and uniformly deeply stained, the nucleus contrasting poorly with the cytoplasm. The location of the lesions in the brain suggests that the pathologic changes are due to anoxemia, since areas which show the most severe changes are those most susceptible to anoxemia, namely, layers 3 and 4 of the cortex (Brodmann), the pallidum, the substantia nigra, the cornu ammonis, especially Sommers' sector, the Purkinje cells, the inferior olivary and dentate nuclei and the dorsal motor nucleus of the vagus.

The increase in glia of the macroglial type and the proliferation of endothelial cells of the meninges point to a decrease in the amount of oxygen, since mesodermic elements proliferate in an atmosphere so deficient in oxygen as to cause severe damage to the ganglion cells. The fact that the glia also shows regressive changes suggests a progressive increase in anoxemia to the point where even it cannot survive.

Of especial interest in these cases were changes in the nuclei that lie in the wall of the body of the ventricle, in the commissura mollis and in the nuclei of the diencephalon. The cells of these nuclei, which are of the hyperchromatic type, showed severe degeneration which appeared to be secondary to the changes in the capillaries.

Theory.—The basis of the cerebral pathologic changes, we believe, is found in the capillaries and in the small venules. The degeneration of the endothelial nuclei and the walls of the vessels permits transudation of fluid; as a result of this there is interference with the transportation of oxygen, so that the final picture is one of cellular anoxemia. This damage is caused by anoxemia of the capillary wall produced by vascular stasis which, in turn, is due to restriction in the volume of blood, with resulting increased viscosity and increased osmotic tension of the blood. The changes in the capillaries throughout the body are not comparable with the changes in the capillaries of the brain. This is accounted for, we believe, by the absence of cerebral vasomotor control to the capillary bed which, in the body, offsets the injurious train of effects resulting from reduced volume of blood.

We do not believe, or mean to intimate, that these changes are specific for diabetic coma. Any condition which produces anoxemia of the capillary wall of the wall of the brain shows the same picture both as to cell change and as to location of the lesion.

In substantiation of this we present 2 cases showing similar pathologic processes in the capillaries and brain; in 1 there was restriction of the blood volume due to massive hemorrhage, and in the other, acute anoxemia following an overdose of morphine.

Dr. Riggs has here found and described lesions in the brain in fatal cases of uncomplicated diabetic coma. We believe that in these 6 cases, which were previously reported as cases of "metabolic deaths," there have been found pathologic changes sufficient to produce the fatal termination. That the lesions are there is indubitable. We can only theorize at this time about the mechanism of their production.

DISCUSSION

Dr. E. Dillon: I wish to point out briefly the frequency of this problem and its relationship to the total number of deaths occurring in the wards of the metabolic department. During the three years from 1931 to 1933, 1,362 diabetic patients were admitted to the wards of the department; of these, 241 died while in the hospital. This is a heavy mortality. In few of these patients the blood chemistry was sufficiently abnormal immediately preceding death for death to be ascribed directly to diabetes. In almost every case normal blood sugar levels were established before the patient died. On the other hand, the majority of the patients died from pathologic conditions which developed as a result of long continued neglect of the diabetes. For instance, 64 per cent of the 241 deaths were due to diabetic gangrene.

There were 121 patients admitted to the hospital in a state of coma or of marked acidosis, that is, with a carbon dioxide-combining power of 29 volumes per cent or less; 46 of these patients died. However, of these 46 patients there were only 12 who had diabetic coma only and no other complicating disease. There were 24 with other diseases so severe that they actually caused death. In these cases the patient had recovered from the state of coma at least forty-eight hours before death occurred, or the condition was obviously overwhelming, as in the case of a patient who died a few hours after admission and while still in a state of acidosis, but in which postmortem examination showed extensive carcinomatosis. In another group of 10 cases a complication was severe enough to precipitate the acidosis, but one could not say that the complication would have caused death without acidosis.

It is the group of cases without complications which is of particular interest, for it has not been possible to explain why the patients have died. Usually they have responded well to treatment, as shown by laboratory tests, that is, the blood sugar has fallen, and there has been a marked rise of carbon dioxide-combining power. Yet about twelve or fourteen hours after treatment was started they have died with rapid pulse, low blood pressure and often marked terminal hyperpyrexia. These cases are discouraging, and I hope that the work of Dr. Dyer and Dr. Riggs will throw light on the cause of death.

Dr. W. W. Dyer: Hyperthermia is almost always present in fatal cases of diabetic coma. When a patient is admitted to the hospital in a state of coma the

temperature is subnormal, from 95 to 96 F. During treatment in fatal cases the temperature rises steadily to 106 or 107 F. As for sweating, while my experience is limited, I have never seen such a patient with hyperthermia sweating or shivering.

DR. M. K. MEYERS: The slides shown by Dr. Riggs present changes which could well occur with anoxemia and hyperthermia. Does Dr. Riggs think there is any relationship between the hyperthermia and the anoxemia? Did Dr. Riggs investigate any cases of tetanus accompanied by hyperthermia to see whether similar changes were present?

DR. H. E. RIGGS: The nuclei showing the greatest pathologic change were the supra-optic and paraventricular. The vascular pathologic change was most marked here and was undoubtedly the basis of the cell damage. It was our observation that large hyperchromatic cells such as comprise the nuclei named were most severely damaged since we also found great damage in the internal medullary lamina and the substantia innominata of Reichert.

In answer to Dr. Meyers, we have studied hyperthermia in a number of conditions and always found the vascular pathologic change and cell damage that I have just described. Always, however, we were able to demonstrate a grave loss of blood volume and a decrease in the systemic blood pressure. Hassin considered that the hyperthermia of "heat stroke" is due to the loss of fluids from excessive perspiration.

When in cases of diabetic coma the blood volume and blood pressure decline to the point of causing cerebral asphyxia by stasis, a vicious circle is established due to the loss of cerebral control of the circulation and respiration, and death is inevitable.

BOSTON SOCIETY OF PSYCHIATRY AND NEUROLOGY

Dec. 20, 1934.

ALBERT W. STEARNS, M.D., *Presiding*

RADICULITIS FOLLOWING INJECTIONS OF ANTITETANUS SERUM: REPORT OF FIVE CASES. DR. JAMES B. AYER.

Despite the fact that paralysis following the use of antitetanus serum has been observed for more than twenty years and appears to be well recognized in France, only a few cases have been recorded in the English and the American literature. While the papers by Foster Kennedy, J. B. Doyle and I. M. Allen called attention to the serious effects of serums of different kinds on the nervous system, the conception that I obtained was that of a considerable diversity of effect. In the words of Allen, foreign serum causes lesions of four different types: radicular, neuritic, polyneuritic and central.

In analyzing 5 cases of paralysis following the injection of antitetanus serum which have come to my attention and that of my associates during the past year, one cannot fail to be struck with the uniformity of effect and even the time intervals between injection, serum sickness and paralysis in these patients. Analysis of the literature with reference solely to tetanus serum (in 1 case reported in the literature and in 2 of the cases here reported antigas bacillus serum also was given) has yielded reports of 40 cases which further strengthen the view that the effect of antitetanus serum is similar, although varying in intensity, in different patients, at all ages and in various countries.

CASE 1 (Courtesy of Dr. Edward Harding).—A student, aged 23, received a puncture wound 2 inches (5 cm.) above the left patella on Jan. 22, 1934. Eighteen hours later he reported to Dr. Harding at the college infirmary, who found the left knee to be swollen with fluid and air. The knee joint was opened, irrigated and closed, without sequelae. Tetanus antitoxin, 1,500 units, with antigas bacillus serum was immediately injected under the left breast. On January 28 there was

a generalized urticarial eruption. On the next day, at 11 p. m., the patient was seized with agonizing pain in the upper part of the right arm, and on the following morning he could not raise this arm.

Examination on January 30 at 6 p. m. (Dr. Ayer) showed the patient to be emotionally and intellectually normal. The cranial nerves were apparently normal. The neck was held well and moved freely in all directions. The left upper extremity and both lower extremities were normal. The sole paralysis was referable to the right shoulder joint; the patient could neither initiate abduction nor hold the arm in abduction, although a feeble contraction of the deltoid muscle could be felt. The right shoulder joint was slightly but definitely swollen, although no limitation of this joint was present nor was there pain on motion. Deep pressure over the shoulder and pressure over the brachial nerves revealed slight tenderness. The biceps and triceps muscles, the muscles of the forearm and hand and the rhomboid and serratus muscles were not weak. There was perhaps diminished perception to pain and touch over the shoulder. Roentgenograms of the shoulder showed nothing abnormal.

A lumbar puncture, performed on February 3 to rule out a diagnosis of poliomyelitis, gave the following result: Fluid, clear and colorless; pressure, 120 mm.; dynamics, normal; cells, 0; globulin, 0; total protein, 87 mg. per hundred cubic centimeters; sugar, 770.5 mg., and colloidal gold curve, 1334445555.

On February 8 electrical tests showed a patchy response of the deltoid muscle to faradic stimulation, but a stronger current was necessary on the right than on the left side. By February 15, sixteen days after the onset of paralysis, the patient could abduct the right arm 40 degrees. He was not seen again until October 23, when he stated that the arm was strong. In spite of this and of almost normal reactions to the electrical tests, there is now obvious atrophy of the right deltoid, supraspinatus and infraspinatus muscles.

Case 2 (Courtesy of Dr. Charles A. McDonald).—A white man, a farm hand, aged 38, rugged as an ox, on April 1, 1934, lacerated his right arm. On the same day tetanus antitoxin was injected into the left arm. Ten days after the injection serum sickness appeared, with rash and edema of the face and also of the larynx. This disappeared in two days (twelve days after the injection of antitoxin), when there was paralysis of the left arm.

Examination (by Dr. McDonald) eighteen days after the accident and injection of antitoxin revealed paralysis of the left deltoid, supraspinatus, infraspinatus and biceps with atrophy and no response to faradism and no signs of toxic-organic disease or of disease of the nervous system, except positive Hinton and Kahn (of long standing) reactions of the blood. The triceps reflex of the left arm was equal to that of the right arm; the biceps reflex of the left arm was 1 plus, that of the right arm, 2 plus. No examination of the spinal fluid was made. On November 4 (eight months after the accident) the patient reported by letter: "At present I am getting along fine and expect it to be O. K. very soon."

Case 3 (Courtesy of Dr. Charles A. McDonald).—An American college boy, aged 17, with a good history as to sickness and operation, on Aug. 28, 1934, had an accident which caused a deep, dirty wound of the nose; tetanus antitoxin, 750 units, was injected into the right arm. Eight days later there was a serum reaction, with hives, fever, pain and aches and general malaise. On the fifteenth day after the accident and the injection there were weakness of the right arm on abduction and external rotation and pain down this arm.

Examination (by Dr. McDonald), twenty days after the accident, revealed no evidence of physical disease and no loss of function of the cranial nerves; the left arm and the left leg were normal in sensorimotor control; the right leg was normal in power, with the knee jerk not as strong as that on the left. The right deltoid, supraspinatus and infraspinatus muscles were weak, atrophied and without response to faradism. The patient could not abduct the right arm or rotate it externally. The right biceps muscle was weaker than the left, but was not as wasted or as weak as the deltoid muscle. The triceps reflex was 2 plus, and the

biceps reflex, 1 plus. The patient also complained of a squeezing pain from the tip of the deltoid muscle to just above the wrist on the flexor surface of the arm. A roentgenogram of the shoulder showed a normal appearance. The Wassermann test was negative; no examination of the spinal fluid was made.

On November 3, forty-six days after the accident, the patient had no pain, no response to faradism, persistent atrophy of the deltoid and spinatus muscles and much less of the biceps muscles with a return of power which he estimated as 25 per cent.

Case 4 (Courtesy of Dr. Henry Viets and Dr. Arthur W. Allen).—A girl, aged 17, first seen on April 14, 1934, had received a gunshot wound of the right forearm and left shoulder two weeks before. The arm and shoulder were filled with shot, which were picked out. There was slight infection, but nothing of great importance. Antitetanus serum was injected into one buttock on the same day and a serum reaction followed, which was not recognized as such at the time.

The following note was received from Dr. Allen: "She (the patient) states that on March 26, 1924, a 410 gage gun, loaded with no. 10 chilled shot, was discharged accidentally while she was sitting with her right hand resting on her left shoulder. The majority of the charge passed through a heavy cushion, the periphery of the charge peppering her in the right hand, neck, face and shoulder. Antitetanus serum was administered on the same day; the dose is not stated. On April 2, while on the train coming to Boston from the South, she felt itchy all over and was very restless; she slept badly that night. The next afternoon she slept soundly in a chair, and when she awakened could not abduct her right arm. Aside from slight infection in a few of the puncture wounds in the forearm where several shot were collected in one spot, the surgical part of the condition rapidly recovered. It was necessary to open two or three abscesses and remove the massed shot. The individual pellets did not produce abscesses."

Examination was made by Dr. Viets, who submitted the following report: "There was nothing unusual except the local condition of the right shoulder. The right deltoid muscle was decidedly weak, although there was some voluntary power. It responded completely to the faradic current, but slowly and with a rather strong current. The supraspinatus and infraspinatus muscles were possibly slightly weak, but this was difficult to test accurately. At the first examination I could not be sure of atrophy, and the results of electrical examination of these muscles were unsatisfactory.

"The patient was seen again on June 21, 1934. In the meantime she had received massage and electrical stimulation, during which there had been a definite increase in the power of the shoulder, and I thought that she had made an excellent recovery. There was, however, definite atrophy of the supraspinatus and possibly a little of the rhomboid and infraspinatus muscles. All movements were possible, but there was a good deal of fatigue when the arm was held directly over the head. The electrical reactions of the deltoid muscle were nearly normal, but I thought there was some slowness in response of the supraspinatus and infraspinatus muscles and possibly of the rhomboid and posterior part of the deltoid muscle.

"The patient has not been seen since that date, but I understand from her father that she spent the summer in the country and was able to do practically everything that she had done before. Her swimming was nearly normal and her playing of golf also. There was, however, a little difficulty in playing tennis and she refrained somewhat from engaging in that game."

Case 5 (Courtesy of Dr. A. R. Kimpton and Dr. Stanley Cobb).—A truck-driver fractured his left elbow in an automobile accident, receiving an extensive laceration of the left arm. He was immediately given tetanus antitoxin in the right arm. After three days infection with gas bacilli developed, and he was given gas bacillus antitoxin, six intravenous injections, of 100 cc. each, into the right arm. There was a marked cutaneous rash after the first injection, which persisted throughout the treatment, although the left arm became gangrenous and had to be amputated.

Three weeks after the accident and at the end of prolonged treatment with antitoxin there began to be weakness of the right arm, first observed when the patient was unable to raise the arm to his head. The weakness has been confined to the upper part of the right arm and shoulder; he has been able to use the wrist and hand perfectly.

Neurologic examination by Dr. Cobb showed the mental reactions to be normal. There was no evidence of invalidism or of any neurosis. The cranium was normal. The cranial nerves were all normal. The right arm showed weakness of the biceps, triceps and deltoid muscles and the abductor and rotator muscles of the shoulder, especially the scapular muscles. There was also some weakness of the abductor muscles of the right shoulder. The motions of the wrist were normal, and there was a strong grip; also the motions of the fingers were normal. These muscles were all abnormally relaxed and felt flabby on palpation. The patient was unable to raise his arm more than halfway to the horizontal position. This was especially obvious when he held the arm in front of him and tried to raise it in that position.

Sensory examination with a needle for pain, with wool for light touch, with pressure with the fingers, with movement of the fingers for position sense and with a tuning fork for vibration sense gave negative results except for a small area over the right shoulder, where there seemed to be a decrease in the vibration sense. Over the right scapula, in the upper part of the infraspinatus muscle, there was a small tender spot. This was the only place where there seemed to be any localized tenderness. There was no tenderness over the nerve trunk.

There was a general increase of all the deep reflexes. This was especially marked in the elbow of the right arm and in both knees. There was no Babinski sign. The abdominal reflexes were active and equal. The ankle jerks were increased. Routine examination of the autonomic nervous system revealed no abnormalities.

It was thought that from clinical examination alone the conditions described represent what is commonly called radiculitis as contrasted with peripheral neuritis; the fact that a single examination of the spinal fluid showed markedly elevated protein content is characteristic of other types of radiculitis. No evidence of damage to the brain, spinal cord or meninges appears in these protocols, nor is there evidence of such in the 40 cases reported in the literature, with the possible exception of the case of a man who had hemiplegia during the height of the serum sickness.

The upper extremities only were paralyzed in our 5 cases, and the deltoid and spinatus muscles appear to have been most severely affected—a point emphasized by others. Analysis of the 45 cases as to the site of paralysis shows: the right upper extremity alone, 21 cases; the left upper extremity alone, 6; both upper extremities, 13, and the serratus muscle (? side), 2. There was hemiplegia (cardiac origin suggested) in 1 case; paralysis of the right lower extremity in 1, and paralysis of all extremities and the neck in 1.

It is not evident why the right upper extremity and the muscles innervated by the fifth cervical root in particular should be selected as points of least resistance in nearly 50 per cent of cases. At least one possible cause can be disposed of: i. e., that paralysis develops in the limb contiguous to the site of injection of serum. Of 24 cases in which adquate data are given, in 8 the paralysis occurred in the limb into which the injection was made, whereas in 16 cases paralysis was on the side opposite to or far from the point of injection.

The intensity of the paralysis varies, but frequently atrophy and a reaction of degeneration are noted. Even in patients with these signs of complete paralysis, restoration of function within a year has been the rule.

Summary: From a study of 5 cases and of 40 cases reported in the literature, one finds a uniform type of paralysis of the upper extremities, usually confined to the right side and frequently involving only the muscles of one shoulder. The paralysis develops suddenly or rapidly during or just after the height of serum sickness and is preceded by excruciating pain involving more nerves than are

subsequently paralyzed. The paralysis follows the distribution of the nerve roots and may be mild or complete, but it is most conspicuous in the muscles supplied by the fifth cervical root. The prognosis appears to be uniformly favorable for complete restoration of function.

Of interest is the finding in 1 case of an increased amount of protein in the spinal fluid, without cells, on the fourth day of paralysis.

DISCUSSION

DR. EDWARD HARDING: This is the first case of the type that I have seen. I have seen antitetanus serum used in thousands of cases abroad, during three years of active hospital service in the British Army, not to mention cases in which it was used in this country, and I have never seen any reaction except the normal cutaneous reaction which appears at the end of eight or nine days. In these cases tests were made before the serum was injected, but there was no reaction. Tests were never carried out in cases abroad.

DR. H. R. VIETS: The only case that I have seen was one similar to the first case mentioned by Dr. Ayer. A brief report of it is incorporated in Dr. Ayer's paper. The patient, a girl aged 17, was accidentally shot in the arm. She was given antitetanus serum on the same day. About a week later she had a serum reaction, followed by severe pain in the right shoulder. The atrophy in this case was not particularly noticeable. The right scapula stood out from the wall of the chest. Under electrical treatment, improvement has taken place with slight residual paralysis. I wish to ask Dr. Ayer about the value of electrical treatment.

DR. C. A. MCDONALD: I saw my first case in April. There is still some atrophy in this case. In another case, which was seen in September, there is extensive atrophy of the deltoid, supinator and pronator muscles. The description of the pain was the same in both cases. It began at night in the elbow and was of a squeezing and pressing type. There are still positive reactions to faradism.

DR. J. LOMAN: I am especially interested in the anaphylactic phase. I recently saw 2 cases of serum reaction in a brother and sister, the former having angioneurotic edema and the latter signs and symptoms of involvement of the cerebrum; in both the symptoms came on acutely and disappeared rapidly. In regard to radiculitis following injections of serum, it may be that anaphylaxis is a factor in its production.

DR. G. C. CANER: I recently saw a young man who experienced severe urticaria a week after the administration of antitetanus serum. A few hours after the appearance of the urticaria there developed severe sharp pain in the back of the neck, radiating over the head. The pain and urticaria continued for months, and in addition there developed a slow monotonous speech, marked difficulty in using the right hand in writing and in buttoning the clothes, weakness of the right leg and attacks of unconsciousness with convulsions. Examination showed asynergy of the right hand and slightly diminished sensation of that hand and leg to vibration and position. Speech was very slow and measured. The right knee jerk was the more active. There was no weakness of the deltoid muscles. It was thought that the symptoms were due to an encephalitic and meningeal reaction, and the case is mentioned to call attention to the possibility of neurologic complications other than the one stressed by Dr. Ayer. Cases have been reported in which the pyramidal tracts are affected.

DR. A. W. STEARNS: At the south department of the Boston City Hospital there is frequent occurrence of postdiphtheritic paralysis. It is sometimes difficult to convince relatives of patients that this paralysis is not due to the antitoxin.

DR. J. B. AYER: With regard to damage to the cerebrum from the injection of serum, Kennedy described such a case in which choked disks were observed after the injection of diphtheria antitoxin and in which a diagnosis of tumor of the brain was entertained until subsidence of the symptoms disproved that diagnosis. In the sole case of possible involvement of the cerebrum from tetanus antitoxin which I found the patient had a bad heart and sudden hemiplegia suggesting a vas-

cular accident rather than encephalopathy. Needless to say, I was surprised not to find evidence of involvement of the brain following the use of antitetanus serum, but the facts overwhelmingly implicate the upper brachial nerve roots.

That other agents cause similar neuritis of the upper brachial roots is likewise true. All have seen this, and Brain, in his textbook, stated that radiculitis most commonly affects the fifth cervical nerve roots; he did not mention serum as the cause. Why serum is so selective, I cannot say.

Concerning the sensory findings, these are minimal. A little anesthesia over the shoulder joint—perhaps only transient—is the most that is usually found; these findings, of course, are following the initial severe pain.

As to etiology, I am almost satisfied that this is an exaggerated serum reaction which has caused, as it were, urticaria of the nerve roots, and the increase in the amount of protein seems to corroborate the suggestion that some congestive process is present.

DR. H. R. VIETS: What does Dr. Ayer advise in the way of treatment?

DR. J. B. AYER: The only treatment is electrical treatment and massage. In the acute stage, i. e., in the first few days, it is possible that drainage of spinal fluid might mitigate a supposed congestion of the nerve roots.

STUDIES IN INTRACRANIAL DYNAMICS. DR. ABRAHAM MYERSON, DR. JULIUS LOMAN and DR. WILLIAM DAMESHEK, with the technical assistance of MISS CAROLINE STEPHENSON and MR. DAVID GOLDMAN.

Pressure conditions, circulation rate and chemical interchange are unquestionably of as great importance in all organs of the body as in the brain and the intracranial space. However, the intracranial pressure and circulation rate are more directly related to clinical syndromes than in any other part of the body, mainly because of the peculiar anatomic construction of the intracranial and vertebral spaces. The intracranial space is often spoken of as a closed box, but this, while relatively true, is greatly modified by the emissary veins which drain off the craniovertebral cavities in a remarkable manner, and probably also by the fact that the cerebrospinal fluid travels along the nerve roots as they leave the craniovertebral cavities and possibly communicates with the lymph spaces elsewhere in the body.

The brain may be conceived of as a solid organ, relatively incompressible, which is traversed not only by the arteries and the veins but probably is penetrated from beginning to end by the cerebrospinal fluid spaces, first, in the septums of the pia-arachnoid and, second, by communications between the perivascular spaces and the subarachnoid space. The arteries enter between the dura and the bone, run for a considerable distance in the subarachnoid space and then break up into a capillary bed. The large arteries do not communicate the changes of their pressure to the intracranial pressure, mainly because of the relative rigidity of their walls, so that changes in arterial pressure are not directly related to changes in intracranial pressure. Such changes as do arise when arterial pressure is increased occur because the arteriole-capillary bed is widened and because of changes in the venous pressure. However, changes in the venous pressure are immediately reflected in changes in the intracranial pressure because the veins also are in direct relationship with the spinal fluid, and since their walls are relatively thin there is consequently an immediate and equal reciprocity between venous pressure and intracranial pressure.

We conceive of the cerebrospinal fluid pressure as a passive resultant of: (1) osmotic pressure, (2) arterial and capillary pressure, (3) venous pressure and (4) those hydrostatic factors which are related to the height of the cerebrospinal fluid column. So far as osmotic pressure is concerned, this is relatively slow to change and is influenced mainly by changes in the osmotic tensions of the blood. That this is of clinical importance is shown by: first, the experiments with hypertonic and hypotonic solutions and, second, the changes which take place in cerebrospinal fluid pressure in cases of nephritis and of other metabolic conditions. Our

experiments have not dealt with this subject except in the case of the effect of insulin, in which after a considerable period of time the cerebrospinal fluid pressure rises, a rise in part due to the depletion of sugar in the blood and also in part due to dilatation of vessels within the brain.

Our experiments have been carried out entirely on human beings unanesthetized, and we have employed as technical factors: (1) puncture of the internal jugular vein and the carotid artery in order to measure the pressure and the chemical content; (2) lumbar and cisternal punctures; (3) use of the tipping table, by which the patient is placed in the head-up or head-down position; (4) the use of the thermo-electric apparatus of Gibbs for measuring changes in circulation rate, and (5) studies in consumption of oxygen within the brain.

As a result of these studies, combined with studies made by distinguished workers, mainly American and English, the following may be stated as the principal factors in the rapid change of conditions of pressure and circulation within the intracranial and vertebral cavities. Postural experiments give the following results:

1. The lateral-recumbent position gives a pressure which may be accepted as a conventional normal but which has no real claim to being established as standard except the ease of obtaining it. Thus, if a patient is placed on his hands and knees, the cerebrospinal fluid pressure in the lumbar and cisternal regions is distinctly lower than when the patient is in the lateral-recumbent position. If the cerebrospinal fluid pressure is taken when the patient is placed horizontally on his back, it is distinctly higher. In each case the change of pressure can be directly related to the relation of the venous column to the heart. The pressure is higher when the patient is in the supine position because of the height of the cardiovertebral venous column. It is lower when he is in the "quadruped" position for the same reason. The sitting position produces changes in the pressure in the lumbar region and in the cistern which may be roughly correlated with the changes in venous pressure which take place in the upper and lower part of the cranial-vertebral venous column.

Craniovertebral Venous Pressures With Change of Posture; Also Cranial Circulation Rate Under the Same Conditions with Reference to the Use of Oxygen Under These Conditions.—In these experiments the patient was placed on a tipping table and was so fastened that he was secure. No pressure was made on the abdomen, chest or neck. In certain experiments he was slowly shifted; in others he was more rapidly shifted in position. Summarization of these experiments shows: In the head-up position the venous and spinal fluid pressures drop and show no compensatory rise. The arterial pressure drops, usually from about 100 within the carotid artery to 60 or 70 mm. of mercury as measured by the intra-arterial technic introduced by us. Very rapidly, however, what we call a compensatory rise takes place. The pressure rises, but not to the level obtained in the horizontal position. At the same time, the circulation rate is diminished. With this slowing up of the stream of blood and the diminished pressure, the oxygen difference between the carotid artery and the internal jugular vein, to wit, that which disappears within the brain per hundred cubic centimeters of blood, increases.

Modifications of the Preceding Experiments in Cases of Cerebral Arteriosclerosis, and the Result of the Use of Drugs.—Patients with cerebral arteriosclerosis and myocardial weakness show the following differences: The compensatory rise of the arterial pressure is absent in these patients or, at any rate, greatly diminished. In other words, the pressure in the carotid artery falls but does rise again. This, we believe, in part at any rate, accounts for the headache, dizziness and other abnormal manifestations so prominent in the symptomatology of persons with cardiovascular disease on effort and in the changing of posture.

When histamine is administered, the head-up position is associated with a more pronounced fall in the pressure in the carotid artery and again a lack of the compensatory rise. In one case in which this drug was administered, the marked drop in the pressure in the carotid artery in the head-up position was

associated with unconsciousness and some clonic movements, which disappeared immediately when the patient was placed in the horizontal position.

Sodium nitrate administered intravenously shortly before change in posture gave much the same result as histamine; there was a great drop in the arterial pressure. There was lack of the compensatory rise, and in 1 case there was unconsciousness. The circulation rate in this case was greatly slowed; at the same time, the use of oxygen was increased.

Results in the Case of a Patient Who Fainted During the Head-Up Shift.—The patient in this case was not warned that any change in posture was to be undertaken. As he was tilted slowly to the head-up position, he fainted. The arterial pressure dropped to 20 mm. of mercury, returning promptly to normal as he was shifted to the horizontal position. On a later occasion the same procedure was carried out except that the patient was told what was going to happen and was reassured as to consequences. The shift this time, made exactly as before, produced no abnormal changes. The blood pressure dropped 20 mm. of mercury. There was a compensatory rise, and the patient remained conscious and comfortable. This, we believe, is the first case ever recorded in which the effects of the emotions of fear and surprise have been graphically recorded in the falling of the pressure in the carotid artery.

Summarization of Experiments with Drugs.—A table is presented showing the results of the various drugs and endocrine products on spinal fluid pressure, venous pressure, arterial pressure, circulation rate and dilatation or constriction of the arterioles within the brain. In general, it may be stated that drugs which dilate the capillaries and the smaller vessels within the brain and in the pia increase intracranial pressure, whereas those which constrict the same blood vessels lower intracranial pressure. In general, the direct mechanism by which these drugs operate is in the change of the caliber of the small vessels. Increased arterial pressure by itself does not raise the intracranial pressure, nor does a decreased arterial pressure lower it. In cases in which increased and decreased pressure have affected spinal fluid, it can be shown definitely that there has been increase in the venous pressure as well, or dilatation or constriction of the smaller vessels.

DISCUSSION

Dr. O. Raeder: I wish to ask a question concerning the case of a patient with dementia praecox who was intelligent and who showed emotion when not warned and did not show it when he was warned. Was this tested on other schizophrenic patients and was the reaction constant?

Dr. Frederic Gibbs: Dr. Myerson has, I think, properly emphasized the importance of the arterial pressure in determining the cerebral blood flow. There has been so much talk about cerebral vasoconstriction and cerebral vasodilatation that one has been inclined to lose sight of the paramount importance of the perfusing pressure. It is clear, however, that as the arterial pressure decreases the cerebral blood flow tends to decrease, and as it increases the cerebral blood flow tends to increase. The second most important factor is the carbon dioxide content of the blood, for carbon dioxide appears to be a specific and powerful dilator of the cerebral vessels. These facts should be kept in mind by the physician who plans to provide supporting treatment for the cerebral circulation.

Dr. H. Powers: I am interested in any information about the use of barbital.

Dr. H. H. Merritt: Dr. Myerson and his co-workers have had the courage to carry out difficult experiments on man which have hitherto been done only on animals. Their work shows that such experiments are practical and harmless. The results in human beings are similar to those previously obtained by other workers in animals. I was greatly interested in the chart which presented the changes in the cerebrospinal fluid pressure, arterial pressure and venous pressure resulting from the intravenous injection of drugs. This chart shows that changes in cerebrospinal fluid pressure can be directly related to changes in venous pressure

or to changes in the size of the vascular bed in the brain. There is nothing in the work of Dr. Myerson or Dr. Loman to indicate that the changes in cerebrospinal fluid pressure can be related to changes in arterial pressure or to the effect of the drug on the so-called "secretion of spinal fluid."

DR. T. J. PUTNAM: This method of studying the factors underlying changes in intracranial pressure opens a possible path of investigation of a great variety of diseases. I wish to raise the question of how formidable the procedure is. Does it disturb the patient very much, or might it be properly employed in a manner comparable to lumbar puncture in the investigation, for example, of the neuroses?

DR. H. H. MERRITT: I know that in many experiments Dr. Myerson has found that cerebrospinal fluid pressure goes well above the venous pressure. Does that hold for veins in the pia? Must they not increase their pressure in comparison or be compressed?

DR. J. LOMAN: In animals a great deal of work has been done on the relationship between the cerebrospinal fluid pressure and the cerebral venous pressure as measured in one of the venous sinuses. Changes in the latter pressure may not give a true picture of the changes in the pressure of the thin-walled veins within the brain. Probably the closest approach to the study of the cerebral venous pressure is that obtained by measuring the intra-ocular venous pressure, as done by Dr. Gibbs in animals and by others in man. By comparing the pressure within these veins and the spinal fluid pressure it may be shown that there is a direct relationship either in the fall or in the rise of the two pressures. As to practical application of the technic used, I think that information in certain clinical conditions may be obtained with relatively little discomfort to the patient. Recently I studied a patient who readily faints when he changes his position from the horizontal to the upright. Measurement of the pressure in the carotid artery in this patient showed a marked drop from 110 to 30 mm. of mercury.

DR. A. MYERSON: In answer to Dr. Raeder's question, most of our work has been on patients with dementia praecox; there have been a few with dementia paralytica and others with arteriosclerosis. These persons faint just as the normal person faints. Perhaps the patients with dementia praecox show more emotion. As to the use of barbital, we have carried out some experiments on its effect. Lowering the blood pressure does not change the venous pressure. There is no change in the cerebrospinal fluid pressure. All barbiturates sharply lower the metabolism and the temperature. If they are given up to anesthesia the metabolism shows a drop of about 30 points. As the patient recovers, the metabolism recovers. Caffeine causes a sharp rise in metabolism, but the exact relationship to cerebrospinal fluid pressure is not clear. Dr. Merritt summed up the matter well. When vessels dilate within the brain and other things remain equal, intracranial pressure rises. When the vessels constrict, intracranial pressure falls. The part of osmosis in relationship to intracranial pressure must be a steady one. However, hypotonic and hypertonic experiments show that drugs which involve the contents of the blood stream involve the cerebrospinal fluid pressure as well. Our experiments with Dr. Gibbs show that intracranial pressure can be raised to 600 mm. without greatly changing the blood flow. In answer to Dr. Putnam's question, I will admit that our technic sounds formidable, but I do not think that a neurosurgeon should worry about little things like puncturing the jugular vein and the carotid artery. We have experienced no difficulty in experiments with patients at the Boston State Hospital, and I believe that a similar experiment with patients suffering with similar neurologic diseases would be as favorable. We have performed experiments on the same patients time and time again with no ill effect. The patient will come off the table smiling. We have seen syncope in only 3 cases and this has occurred after the simplest experiments, namely, the tipping experiments. I do not see why, with the proper selection of patients and careful observance of the ordinary rules of asepsis and humanity, that this technic could not be used as a routine at the Boston City Hospital.

Book Reviews

Behavior Mechanisms in Monkeys. Behavior Research Fund Monograph. By Heinrich Kluever. Price, $4. Pp. 387, with 52 illustrations. Chicago: University of Chicago Press, 1933.

In this valuable book Kluever presents experimental work and opinions concerning his investigation of the behavior of monkeys. He attempts to separate theoretical discussion from the description of experiments by his division into chapters. Three chapters contain theoretical matters. In these Kluever discusses the significance of his experimental results and the methods he has devised and points to lines of further research. He analyzes his own opinions concerning a wide range of psychologic questions, such as figure and ground, the field, abstraction, generalization and intelligence. Two short chapters present the history of the animals used and the chronological order of the experiments. The bulk of the book is made up of two chapters in which are described in painstaking detail his experiments with monkeys.

In most of the experiments, Kluever used what he calls the "method of equivalent stimuli." A monkey is trained to choose, for example, the heavier of two boxes (otherwise exactly similar) that are obtainable by pulling in certain strings. During training the monkey is rewarded after pulling in the correct box by finding a piece of banana inside and is punished for an error by finding none. After training has become effective the situation is changed in one way or another in order to discover under what conditions the monkey will still pull in the heavier box. It was found that in spite of differences from the training situation in respect to the absolute or relative weights of the boxes, their appearance, their position in relation to the animal, their affective value (a caged rat was attached to the box) or the number of boxes presented, the monkey still pulled in the heavier box. All these situations are therefore "equivalent" to that presented during training, whereas certain other situations are "non-equivalent" in that they somehow prevent the monkey from making the proper choice.

Kluever hopes by this sort of experiment to find how the world as seen by the monkey differs from the world as seen by man. From such an experiment he concludes that monkeys can respond to something as abstract as the fact that one object is heavier than another, no matter what the exact weights used. It is interesting that during training each monkey spontaneously invented a method of comparing the two weights by pulling alternately at the two strings. In other experiments Kluever determined that monkeys react differently in response to pairs of noises differing in quality and to differences in such attributes of visual phenomena as area, brightness, color and intermittence.

In another type of experiment he investigated the monkey's world by presenting to it a problem to be solved by the use of tools. Food is placed out of reach of the animal, and tools are available with which to reach it. The monkey chiefly tested in this way succeeded in solving problems of considerable complexity. For example, she used a wire to secure a short stick with which she was able to secure another stick long enough to reach the food and draw it in to her. From these experiments Kluever concludes that at least some species of monkey are able to use and, indeed, to invent and fabricate tools with an intelligence comparable to that of apes.

Kluever's object in all these experiments was to establish a body of knowledge about the psychologic phenomena of monkeys which is based on carefully conducted experiments. In his work he apparently took great care with controls. In his discussions he frequently points to fallacies in methods formerly used and to dangers of faulty analysis of experimental data. In making claims on the basis of his experimental results he takes such a conservative attitude that after many pages of descriptions of experiments his conclusions are rather meager. He often belittles

the results so stated and points to further work necessary for clarifying his problems. Indeed, as one of the weaknesses of the book is the meagerness of actual conclusions, so its strength lies in its suggestiveness of paths of future inquiry. Incidentally, to his work he has invented a number of methods and suggests their further development along special lines. All this is in line with true scientific method. He is constantly looking forward to a body of knowledge and a set of methods which will facilitate investigation in many fields and help to solve some of the fundamental problems of the mind.

In describing experiments he is systematic, careful and fairly concise, but in theoretical discussion he loses coherence and is obscure.

Dr. K. S. Lashley has written an introduction to the book. He comments on the importance of the study of subhuman primates for understanding human behavior. Kluever's monograph, he writes, "sets a new standard for analytic studies of behavior," bringing forth "for the first time something approaching a complete picture of the perceptual world of an animal." He encourages such studies with lower animals. "The most immediate value of the study," he writes, "is in laying a foundation for investigations of the neurophysiology of behavior."

The editor of the series in which this book appears (the Behavior Research Fund Monographs), Ernest W. Burgess, writes a foreword in which he praises Kluever as embodying "in an unusual degree the elements essential to the best scientific investigation in any field."

Book Notices

General Experimental Psychology. By A. Gordon Bills. Price, $4. Pp. 640, with 116 illustrations. New York: Longmans Green & Co., 1934.

In this era of "science consciousness" the demand for new facts, new theories and new experiments is great; the supply is continuous. Professor Bills of the University of Chicago steps from his laboratory to serve as a scribe for his colleagues in order that the youth of this land may be served the latest when they sign up for a course in experimental psychology. To carry out his aim "to encompass a somewhat wider subject matter than has heretofore been covered in experimental textbooks, in order to include the more significant results of recent research," the author has been discriminating in his choice of a few from the many for his six hundred and forty page book.

The arrangement of the matter is systematic. The principal divisions are six: "Sensory Processes," "The Perceptual Process," "Learning and Memory," "Association and Thought," "Work and Fatigue" and "Emotional and Affective Processes." Learning, which in many current texts is reduced through scant attention to a low rank, is here duly emphasized.

Throughout the pages are scattered an abundance of diagrams, charts and illustrations of apparatus. Each chapter has a complete bibliography. The student will find helpful the discussion of the postulates and methods of experimental psychology in the introduction. The laboratory worker will appreciate the appendixes: "Essential Statistics Methods for Experimental Psychology" and "The Psychophysical Method." There are separate indexes for the authors and the subjects mentioned. The exposition is direct and lucid.